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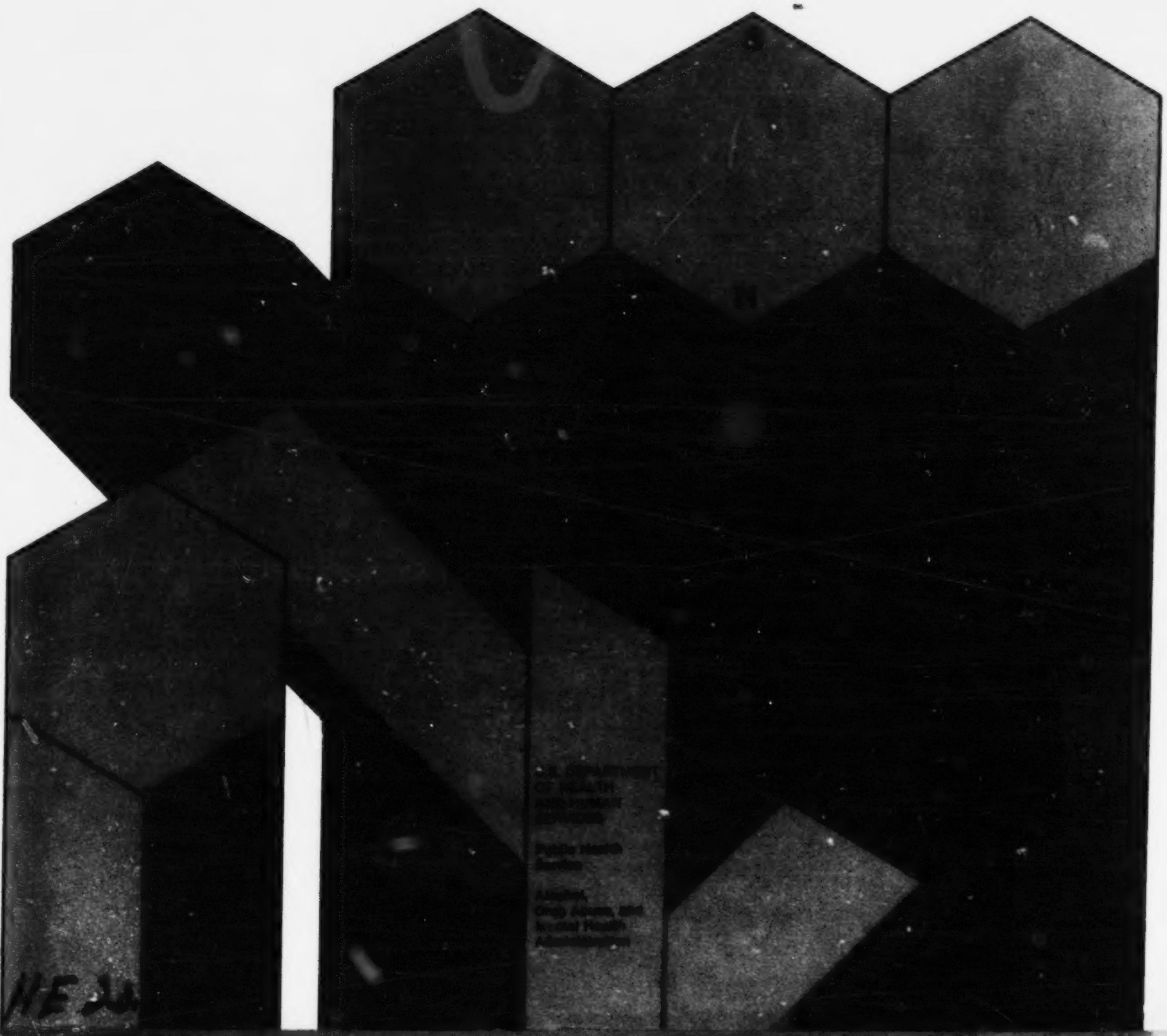

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Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

002633 Allan, R. D.; Curtis, D. R.; Headley, P. M.; Johnston, G. A. R.; Lodge, D.; Twitchin, B. Dept. of Pharmacology, Australian National University, P.O. Box 334, Canberra City, A.C.T 2601, Australia **The synthesis and activity of cis- and trans-2-(aminomethyl) cyclopropanecarboxylic acid as conformationally restricted analogues of GABA.** Journal of Neurochemistry. 34(3):652-656, 1980.

Two GABA analogues, cis-trans-2(aminomethyl)-cyclopropanecarboxylic acid (CAMP) and trans-2-(aminomethyl)-cyclopropanecarboxylic acid (TAMP), were synthesized and tested for biological activity. When administered microiontophoretically, TAMP was more potent than GABA as a bicuculline sensitive depressant of the firing of cat spinal neurons in vivo, but CAMP was less potent than GABA and not sensitive to bicuculline. TAMP was a weak inhibitor of sodium dependent uptake of GABA rat cerebral cortex and was a substrate for GABA:2-oxoglutarate aminotransferase activity in extracts of rat brin mitochondria. CAMP did not influence GABA uptake or aminotransferase activity, and neither isomer reduced glutamate decarboxylase activity in rat brain homgenates. Both cyclopropane isomers inhibited the sodium independent binding of GABA to synaptic membranes from rat brain. Results indicate that extended rather than folded conformations of GABA are active at most GABA recognition sites within the mammalian CNS. 21 references. (Author abstract modified)

002634 Armstrong, D. M.; Pickel, V. M.; Joh, T. H.; Reis, D. J.; Miller, R. J. Dept. of Neurology, Laboratory of Neurobiology, Cornell University Medical College, New York, NY 10021 **Immunocytochemical localization of catecholamine synthesizing enzymes and neuropeptides in area postrema and medial nucleus tractus solitarius of rat brain.** Journal of Comparative Neurology. 196(3):505-517, 1981.

The catecholaminergic and peptidergic neurons in the area postrema and adjacent portion of the medial nucleus tractus solitarii (mNTS) were characterized by the immunocytochemical localization of the catecholamine synthesizing enxyme tyrosine hydroxylase (TH), dopamine beta-hydroxylase (DBH) and phenylethanolamine-N-methyltransferase (PNMT) and two neuropeptides, substance-P and (Leu5)-enkephalin. The catecholamine synthesizing enzymes TH and DBH, found jointly only in noradrenergic and adrenergic neurons, were localized in cells having a similar morphology and topographical distribution. These cells were located throughout the rostrocaudal and dorsoventral extent of the area postrema as well as in neurons within the mNTS. Based on data concerning biosynthetic enzyme markers and neuropeptide localization, it is suggested that neurons within the area postrema contain noradrenalin and enkephalin and that the afferent axons contain substance-P, adrenalin, and probably noradrenalin. 30 references. (Author abstract modified)

002635 Barden, N.; Dupont, A.; Labrie, F.; Merand, Y.; Rouleau, D.; Vaudry, H.; Boissier, J. R. MRC Group in Molecular Endocrinology, Centre Hospitalier, Universite Laval, Quebec G1V AG2, Canada **Age-dependent changes in the beta-endorphin content of discrete rat brain nuclei.** Brain Research. 208(1):209-212, 1981.

Concentrations of beta-endorphin were measured by radioimmunoessay in discrete brain nuclei of young (3 months) and old (24 months) rats. The beta-endorphin content of all major structures known to contain this peptide, with the exception of the eminence, is reduced (at a level which is approximately 50% of control values) in the old rats. The highest concentration of beta-endorphin was found in the arcuate nucleus, the hypothesized exclusive location of cell bodies of the brain beta-endorphinergic system. Since opiate peptides injected intracerebrally stimulated prolactin secretion, it is difficult to reconcile the decrease in brain beta-endorphin levels with the increased plasma prolactin levels of old rats. 25 references. (Author abstract modified)

002636 Barker, Steven A.; Harrison, Robert E. W.; Monti, John A.; Brown, George B.; Christian, Samuel T. Neurosciences Program, Dept. of Psychiatry, University of Alabama, Birmingham, AL 35294 **Identification and quantification of 1,2,3,4-tetrahydro-beta-carboline, 2-methyl-1,2,3,4-tetrahydro-beta-carboline, and 6-methoxy-1,2,3,4-tetrahydro-beta-carboline as in vivo constituents of rat brain and adrenal gland.** Biochemical Pharmacology. 30(1):9-17, 1981.

The identification and quantification of three 1,2,3,4-tetrahydro-beta-carbolines as normal constituents of rat brain and adrenal gland, using combined gas chromatographic/mass spectrometric techniques, are reported. Qualitative analyses of these tissues led to the identification of 1,2,3,4-tetrahydro-beta-carboline (THBC), 2-methyl-THBC (2-MTHBC), and 6-methoxy-THBC (6-MeOTHBC), as determined by observed peak retention times, mass fragments, and ion mass ratios. Quantitative analyses using deuterated internal standards, gave the following results: THBC (ng/g wet wt) in brain = 17.5, adrenal = 500.3. 6-MeOTHBC (ng/g wet wt) in brain = 35.6, adrenal = 1113.7. Mechanisms for the formation of these beta-carbolines as well as their possible function in vivo are discussed. 43 references. (Author abstract)

002637 Becker, Kenneth L.; Silva, Omega L.; Post, Robert M.; Ballenger, James C.; Carman, John S.; Snider, Richard H.; Moore, Charles F. Section of Endocrinology, V. A. Medical Center, Washington, DC **Immunoreactive calcitonin in cerebrospinal fluid of man.** Brain Research. 194(2):598-602, 1980.

Immunoreactive calcitonin (iCT) was detected in the cerebrospinal fluid (CSF) of 27 normal human Ss. Determinations made using an antibody with midportion recognition indicated a mean iCT content of 28pg/ml in the CSF and 89pg/ml in the serum of Ss, with a CSF/serum distribution ratio of 0.31. There were no significant correlations between CSF iCT or serum iCT and the calcium, magnesium, phosphate, sodium, potassium, or chloride contents of the CSF or serum. 33 references. (Author abstract modified

002638 Glazer, E. J.; Basbaum, A. I. Dept. of Anatomy, University of California, San Francisco, CA 94143 **Immunohistochemical localization of leucine-enkephalin in the spinal cord of the cat: enkephalin-containing marginal neurons and pain modulation.** Journal of Comparative Neurology. 196(3):377-389, 1981.

The spinal cord distribution of the endogenous opioid peptide leucine-enkephalin in the cat was examined using immunohistochemical techniques. The distribution of nerve processes was studied in untreated cats; colchicine was administered to study the distribution and morphology of spinal enkephalin containing perikarya. Enkephalin immunoreactive processes were greatest in laminae I and II (marginal layer and substantia gelatinosa) of the superficial dorsal horn. In many sections, the outer substantia gelatinosa (SG), lamina IIA, was discernibly less immunoreactive than were laminae I or IIb. Despite previous reports in the rat emphasizing the enkephalin somata of the SG, in the cat the majority of superficial dorsal horn enkephalin somata were found in the marginal layer. It is suggested that many spinal enkephalin neurons, generally thought to be local circuit neurons, project rostrally, to other spinal levels and perhaps to the brainstem and/or thalamus. 76 references. (Author abstract modified)

002639 Johnson, Robert Paul; Sar, Madhabananda; Stumpf, Walter E. Sar: Dept. of Anatomy, Div. of Health Affairs, University of North Carolina, Chapel Hill, NC 27514 **A topographic localization of enkephalin on the dopamine neurons of the rat substantia nigra and ventral tegmental area demonstrated by combined histofluorescence-immunocytochemistry.** Brain Research. 194(2):566-571, 1980.

A combined histofluorescence/immunocytochemistry technique was used to study the anatomical relationships of enkephalin and dopamine terminals and to examine the fibers in close relation to the dopamine neurons of the substantia nigra and ventral tegmental area. In general, enkephalin was localized near dorsal dopamine cells that project to cortical areas, whereas ventral dopamine cells projecting to striatal structures received less enkephalin innervation. 23 references.

002640 Kelly, Paul A. T.; McCulloch, James. McCulloch: Wellcome Surgical Institute, University of Glasgow, Glasgow, G61 1QH, Scotland **Heterogeneous depression of glucose utilization in the caudate nucleus by GABA agonists.** Brain Research. 209(2):458-463, 1981.

Local cerebral glucose utilization in the rat caudate nucleus has been examined following the intravenous administration of the GABA agonists muscimol and THIP. Although glucose utilization was reduced throughout the striatum following GABA agonists, the magnitude of the reductions in the lateral portion of the nucleus were markedly greater than in other portions of the caudate nucleus. This medial/lateral heterogeneity in response to GABA agonists contrasts with the known rostral/caudal heterogeneity in the distribution of biochemical markers for GABA. 22 references. (Author abstract)

002641 Lewis, Michael E.; Mishkin, Mortimer; Bragin, Evgeni; Brown, Roger M.; Pert, Candace B.; Pert, Agu. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Opiate receptor gradients in monkey cerebral cortex: correspondence with sensory processing hierarchies.** Science. 211(4487):1166-1169, 1981.

In order to obtain information on the possible functions of endogenous opiates in the primate cerebral cortex, the distribution of mu-like opiate receptors (which selectively bind 3H labeled naloxone) and omega-like opiate receptors (which selectively bind 3H labeled D-Ala2, D-Leu5-enkephalin) throughout the cerebral cortex of the monkey was examined. Stereospecific (3H)naloxone binding sites increased in a gradient along hierarchically organized cortical systems that sequentially process modality specific sensory information of a progressively more complex nature. Specific (3H)enkephalin binding sites, in contrast, were relatively evenly distributed throughout the cerebral cortex. These results, in combination with electrophysiological studies of monkeys and humans, suggest that mu-like opiate receptors may play a role in the affective filtering of sensory stimuli at the cortical level, that is, in emotion induced selective attention. 29 references. (Author abstract)

002642 Massotti, M.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The regulation of benzodiazepine recognition sites by endogenous modulators.** Advances in Biochemical Psychopharmacology. 26:19-26, 1981.

The regulation of benzodiazepine recognition sites by endogenous modulators is discussed, and a simple method to solubilize benzodiazepine recognition sites from crude synaptic membrane, and a rapid procedure to remove from the solubilized benzodiazepine sites traces of GABA or other interfering material of small molecular weight are described. Results indicate that rat brain contains a considerable inhibitory activity of 3H-diazepam binding which is pronase sensitive and has a molecular weight higher than that of purines, nicotinamide, or beta-carbolin carboxylate. The activity that can be extracted from the brain is considerable. From 100 mg of rat brain cortex, enough activity to displace 1pmole of diazepam, bound to the purified binding protein, can be extracted. This material is thermostable, pronase sensitive, and acts like an apparent competitive inhibitor of 3H-diazepam binding. Its molecular weight is estimated to be larger than 1,800 daltons. 13 references. (Author abstract modified)

002643 Mohler, H.; Wu, J. -Y.; Richards, J. G. Pharmaceutical Research Dept., Hoffmann-La Roche, CH-4002 Basle, Switzerland **Benzodiazepine receptors: autoradiographical and immunocytochemical evidence for their localization in regions of GABAergic synaptic contacts.** Advances in Biochemical Psychopharmacology. 26:139-146, 1981.

Autoradiographical and immunocytochemical evidence of the localization of benzodiazepine receptors in regions of GABAergic synaptic contacts is reviewed. The demonstration of benzodiazepine receptors in GABAergic synapses is claimed to bridge the gap between the electrophysiological evidence emphasizing the involvement of GABAergic synaptic transmission in the action of benzodiazepines, and the biochemical evidence emphasizing benzodiazepine receptors as the site of action for this group of drugs. The possibility that some benzodiazepines are localized in nonGABAergic synaptic contact regions is noted. 7 references.

002644 Palacios, Jose M.; Unnerstall, James R.; Young, W. Scott, III; Kuhar, Michael J. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Radiohistochemical studies of benzodiazepine and GABA receptors and their interactions.** Advances in Biochemical Psychopharmacology. 26:53-60, 1981.

Radiohistochemical studies of benzodiazepine receptors and GABA receptors and their interactions are described. Throughout the rat CNS, both benzodiazepine and GABA receptors were found to have heterogeneous distributions, which are different from each other and different from other receptor distributions. Both benzodiazepine receptors and high affinity GABA receptors showed striking variation in their distribution in the brain. Although some areas showed high levels of both benzodiazepine and high affinity GABA receptors, many areas showed elevations in the number of only one of the receptors. Since there is not a fixed ratio between the quantity of benzodiazepine and GABA receptors in all areas, it is suggested that there is not a simple constant relationship between the two receptors. 34 references.

002645 Paul, S.; Marangos, P; Brownstein, M.; Skolnick, P. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Demonstration and characterization of an endogenous inhibitor of GABA-enhanced (3H)-diazepam binding from bovine cerebral cortex.** Advances in Biochemical Psychopharmacology. 26:103-110, 1981.

The demonstration and characterization are described of low molecular weight substance(s) in bovine brain which is 10-fold to 20-fold more potent in antagonizing the GABA enhanced binding of (3H)diazepam than in antagonizing basal (nonGABA enhanced) binding of (3H)diazepam to receptor sites. The

GABA mediated enhancement of benzodiazepine receptor affinity may represent an important means of expressing the actions of both pharmacological agents and endogenous ligands. Using an aqueous extraction procedure, two peaks were eluted from a Biogel P-6 column which antagonized the GABA enhanced increase in (3H)diazepam binding. The substance(s) contained in one of the peaks (peak II) proved to be far more potent in antagonizing this effect than in displacing (3H)diazepam from non-GABA stimulated membranes, suggesting a specificity for the GABA/benzodiazepine coupling site rather than the benzodiazepine recognition site. 17 references.

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

002646 Hunkeler, W.; Mohler, H.; Pieri, L.; Polc, P.; Bonetti, E. P.; Cumin, R.; Schaffner, R.; Haefely, W. Pharmaceutical Research Dept., F. Hoffmann-La Roche & Co., Ltd., CH-4002 Basel, Switzerland **Selective antagonists of benzodiazepines.** Nature. 290(5806):514-516, 1981.

The main properties of a representative (Ro 15-1788) of a novel class of specific benzodiazepine antagonists are described. Compounds were discovered while working on a series of imidazodiazepines, which are potent inhibitors of the specific high affinity binding of 3H-diazepam to brain synaptosomal fractions, but which fail to produce any of the behavioral and neurological effects typical of benzodiazepines. The discovery of such antagonists is analogous to that of opiate antagonists and should be useful as antidotes for intoxications involving overdoses of benzodiazepines. As research tools, it is expected that Ro 15-1788 and other specific benzodiazepine antagonists will be useful in defining the structural properties required for molecules to be recognized and bound by benzodiazepine receptors and to induce or prevent those conformational changes in the receptor protein that result in the typical enhancement of GABAergic transmission. 20 references.

002647 Krogsgaard-Larsen, P.; Falch, E.; Schousboe, A.; Curtis, D. R.; Lodge, D. Dept. of Chemistry BC, Royal Danish School of Pharmacy, DK-2100 Copenhagen O, Denmark **Piperidine-4-sulphonic acid, a new specific GABA agonist.** Journal of Neurochemistry. 34(3):756-759, 1980.

Piperidine-4-sulphonic acid (P4S) depressed the firing of cat spinal neurons in vivo with a potency comparable to that of 3-aminopropranesulphonic acid and greater than that of GABA itself. P4S was also a potent inhibitor of binding to GABA receptor sites in rat brain homogenates, but had no a detectable affinity for the neuronal and glial GABA transport system in mouse brain. Results indicate that P4S is a potent and specific agonist for GABA postsynaptic receptor sites. 27 references.

002648 Leysen, J. E.; Awouters, F.; Kennis, L.; Laduron, P. M.; Vandenberk, J.; Janssen, P. A. J. Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Receptor binding profile of R 41 468, a novel antagonist at 5-HT2 receptors.** Life Sciences. 28(9):1015-1022, 1981.

For a new antiserotonergic agent, R 41 468 and 13 reference compounds with alleged antiserotonergic activity, the receptor binding profile is reported, comprising Ki values measured in 10 different receptor binding models. R 41 468 appears to be a particularly selective agent with respect to differentiation between two 5-hydroxytryptamine (5-HT) receptor models; it primarily displays high binding affinity for 5-HT2 receptors and is inactive at 5-HT1 receptors. Apart from R 41 468, no other compound showed a similar selectivity toward 5-HT2 receptors. In the 5-HT2 and 5-HT1 receptor binding models, the D-receptor antagonist phenoxybenzamine was weakly active and the M-receptor antagonist morphine was inactive. It is concluded that R 41 468 is a particularly suitable tool to antagonize 5-HT action mediated by 5-HT2 receptors. 29 references. (Author abstract modified)

002649 Patrick, Robert L. Neuroscience Section, Division of Biology and Medicine, Brown University, Providence, RI 02912 **Phenylethylamine effects on dopamine synthesis. Structure-activity relationships.** Biochemical Pharmacology. 30(2):141-146, 1981.

The effects of various substituents on phenylethylamine induced and amphetamine induced alterations in dopamine synthesis were studied in rat brain synaptosomal preparations isolated from the corpus striatum. The stimulation of synthesis normally observed with phenylethylamine and amphetamine was converted into inhibition by the addition of a p-hydroxy substituent on the ring. Beta-hydroxy substitution on the side chain somewhat diminished, but did not prevent, synthesis stimulation, whereas the presence of both the beta-hydroxy and p-hydroxy substituents appeared to increase the inhibitory effects. The data suggest that the parent phenylethylamine compounds interact with an intracellular regulatory site, possibly related to calcium flux and/or dopamine release, that is not affected by the p-hydroxy derivatives. 28 rerferences. (Author abstract modified)

002650 Ronai, Andras Z.; Berzetei, Ilona P.; Szekely, Jozsef I.; Miglecz, Erzsebet; Kurgyis, Jozsef; Bajusz, Sandor. Institute for Drug Research, P.O. Box 82, H-1325 Budapest, Hungary **Enkephalin-like character and analgesia.** European Journal of Pharmacology. 69(3):263-271, 1981.

The opioid activities of enkephalin analogues with amino pentane-sulfonic/phosphonic acid at position 5 were studied in the rat tail flick test and in electrically stimulated guinea-pig ileum and mouse vas deferens preparations. The compounds could be classified as met-enkephalin like, beta-endorphin like, (nor)morphine like, or intermediate on the basis of their in vitro activities. Correlation of the in vitro activities with analgesic activity in male CFY rats indicated that enkephalin like character may hinder the expression of analgesic activity after intracerebroventricular or i.v. administration. 45 references. (Author abstract modified)

002651 Vaatstra, W. Jan; Deiman-Van Aalst, Wilhelmina M. A.; Eigeman, Leo. Dept. of Pharmacology, Duphar B.V., P. O. Box 2, Weesp, The Netherlands **DU 24565, a quipazine derivative, a potent selective serotonin uptake inhibitor.** European Journal of Pharmacology. 70(2):195-202, 1981.

The quipazine derivative 6-nitro,2-(1-piperazinyl)quinoline (DU-24565) was a potent and selective inhibitor of 5-hydroxytryptamine (5-HT) uptake in Wistar rat brain synaptosomes and blood platelets. The brain 5-HT depletion induced by p-chloroamphetamine was antagonized by DU-24565 with a median effective oral dose of 0.7mg/kg. A 1mg/kg oral dose of DU-24565 antagonized the decrease in 5-HT induced by 4,alpha-dimethyl-m-tyramine and reduced 5-HT turnover. The compound also potentiated the behavioral effects of 5-hydroxytryptophan (5-HTP) in mice, potentiated the temperature increases caused by 5-HTP in rabbits, and had little or no effect in noradrenaline potentiation tests. Results indicate that DU-24565 may be useful as an antidepressant and as a tool in the study of the role of 5-HT in the CNS. 21 references. (Author abstract modified)

002652 Zetler, G. Institut fur Pharmakologie, Medizinische Hochschule Lubeck, D-2400 Lubeck, West Germany **Central depressant effects of caerulein and cholecystokinin octapeptide (CCK-8) differ from those of diazepam and haloperidol.** Neuropharmacology. 20(3):277-283, 1981.

Caerulein and cholecystokinin octapeptide (CCK-8) produced dose dependent catalepsy and antagonized methylphenidate induced stereotypy in male NMRI mice. The peptides increased the seizure threshold dose for picrotoxin, but not for bicuculline or pentetrazol. Caerulein and CCK-8 shared some but not all typical pharmacological properties of diazepam and haloperidol, but evidenced a generally, more potent central activity than did the reference drugs on a molar basis. 38 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002653 Albertson, T. E.; Peterson, S. L.; Stark, L. G.; Lakin, M. L.; Winters, W. D. Dept. of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **The anticonvulsant properties of melatonin on kindled seizures in rats.** Neuropharmacology. 20(1):61-66, 1981.

The anticonvulsant properties of melatonin were investigated by testing acute doses of melatonin against two types of kindled seizures in the rat (electrically kindled amygdaloid seizure and pentylenetetrazol kindled seizures). Against the electrically kindled amygdaloid seizure, melatonin significantly reduced afterdischarge length at a nonsedative dose, but failed to modify seizure rank scores. Melatonin significantly reduced seizure rank socres in pentylenetetrazol kindled animals. It appears that melatonin is most effective against the kindled pentylenetetrazol seizure, and somewhat less effective against the electrically kindled amygdaloid seizure. It is noted that this is the first report of a substantial anticonvulsant property of parenteral malatonin in two animal models of epilepsy. 49 references. (Author abstract modified)

002654 Alphs, L.; Heller, A.; Lovenberg, Walter. Lovenberg: Section on Biochemical Pharmacology, Hypertension-Endocrine Branch, NHLBI, Building 10, Room 7N262, Bethesda, MD 20205 **Adrenergic regulation of the reduction in acetyl coenzyme A:arylamine N-acetyltransferase activity in the rat pineal.** Journal of Neurochemistry. 34(1):83-90, 1980.

Pharmacologically active agents were used to study the mechanisms that control acetyl-coenzyme-A:arylamine N-acetyltransferase (NAT) activity in the pineal gland of male Sprague-Dawley rats. Results showed that the decrease in NAT activity induced by light could be mimicked by in vivo administration of certain alpha-adrenergic agonists and blocked by alpha-adrenergic antagonists. Control over the rapid reduction in NAT activity appeared to be modulated by two distinct receptors with alpha-adrenergic characteristics and these receptors appeared to be located in the CNS. 16 references. (Author abstract modified)

002655 Altstein, Miriam; Dudai, Yadin; Vogel, Zvi. Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Benzodiazepine receptors in chick retina: development and cellular localization.** Brain Research. 206(1):198-202, 1981.

The development and cellular localization of benzodiazepine receptors in chick retina were examined. Benzodiazepine receptors are present in high concentration in the chick retina. Their pharmacological properties are similar to those of the benzodiazepine receptors present in the brain. The retina receptors appear prior to, as well as during, the period of synaptogenesis. In the newborn chick retina, the receptors are localized in the inner synaptic layer, probably on or close to synaptic connections. 19 references. (Author abstract modified)

002656 Altstein, Miriam; Mittman, Scott; Vogel, Zvi. Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **The effect of barbiturates on the degradation of enkephalin by brain enzymes.** Life Sciences. 28(2):185-191, 1981.

The effects of barbiturates on the degradation of enkephalin by brain enzymes were investigated. It is reported that the activity of the enzyme enkephalinase is inhibited by various barbiturates in a physiological range of concentrations and in accordance with their physiological potency (secobarbital greater than pentobarbital greater than phenobarbital greater than barbital). The N-1-methyl substituted barbiturates, methohexital and hexobarbital, as well as barbituric acid have very low or no inhibitory activity. The barbiturates do not inhibit two other brain enzymes shown to degrade enkephalin, i.e. the enkephalin degrading aminopeptidase and enkephalinase-B. 18 references. (Author abstract modified)

002657 Ambron, Richard T.; Sherbany, Ariel. A.; Schwartz, James H. Dept. of Anatomy, Division of Neurobiology and Behavior, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **Distribution of membrane glycoproteins among the organelles of a single identified neuron of Aplysia. II. Isolation and characterization of a glycoprotein associated with vesicles.** Brain Research. 207(1):33-48, 1981.

The use of anisomycin, an inhibitor of protein synthesis, to examine whether component-I (glycoprotein-I with a molecular weight of 180,000 Daltons) is a constitutent of somatic compound vesicles is reported. In the presence of the drug, (3H)N-acetylgalactosamine injected into R2 (the giant cholinergic neuron in the abdominal ganglion of Aplysia) is incorporated almost exclusively into component-I. Quantitative electron microscopic radioautography of treated cells shows a marked increase in the proportion of silver grains over compound vesicles and a decrease in labeling of other organelles compared with untreated cells. Analysis of component-I, isolated using the chaotropic agent lithium diiodosalicylate, shows it to contain fucose, N-acetylgalactosamine, and N-acetylglucosamine. Proteolytic digestion with pronase yields a complex pattern of glycopeptides. The proportion of (3H)N-acetylgalactosamine in these glycopeptides is altered in the presence of anisomycin. These results suggest that large carbohydrate chains are elaborated within the endoplasmic reticulum and that smaller chains are added in the Golgi region or on the membrane of the compound vesicle. 31 references. (Author abstract modified)

002658 Anden, N. E.; Leander, S. Dept. of Pharmacology, University of Goteborg, Goteborg, Sweden **Effects of 4-aminopyridine on the turnover of monoamines in the central nervous system of the rat.** Journal of Neural Transmission. 44:1-12, 1979.

The effects of 4-aminopyridine (4-AP) on the turnover of 5-hydroxytryptamine, dopamine, and noradrenaline in the central nervous system of rats were studied by means of amine disappearance following inhibition of tryptophan or tyrosine hydroxylase. It was found that 4-AP (3mg/kg i.p) did not change the utilization of 5-hydroxytryptamine or dopamine, but markedly accelerated that of noradrenaline in the brain and in the spinal cord. The stimulatory effect of 4-AP was dependent completely on nerve impulses, since no effect was observed following an acute section of the noradrenaline nerves to the spinal cord. The effect of 4-AP was blocked by the alpha-adrenoreceptor stimulating agent, clonidine. Pentylenetetrazole, at a dose producing similar behavioral changes as 4-AP, caused only a slight stimulation of the noradrenaline turnover. It is concluded that 4-AP may enhance the flux of calcium ions into a nerve terminal during depolarization and thus increase the release of noradrenaline, whereas this process may be of less importance in the dopamine and the 5-hydroxytryptamine nerves. (Journal abstract)

002659 Antelman, Seymour M.; Chiodo, Louis A. Western Psychiatric Institute and Clinic, University of Pittsburgh, School of Medicine, Pittsburgh, PA **Repeated antidepressant**

treatments induce a long-lasting dopamine autoreceptor subsensitivity: is daily treatment necessary for clinical efficacy? Psychopharmacology Bulletin. 17(1):92-94, 1981.

The hypothesis that tricyclic antidepressants (TCA) induce a subsensitivity of presynaptic dopamine (DA) receptors was investigated in rats via single unit studies employing change in DA activity in response to a presynaptic dose of apomorphine as an index of DA autoreceptor sensitivity. Results clearly indicate that subsensitivity of DA autoreceptors must be seriously considered in thinking about transmitter mechanisms which might underlie the therapeutic efficacy of both TCAs and electroconvulsive shock (ECS). It is noted that the ability of acute TCA and ECS treatments to trigger the same subsensitivity effects as those obtained with daily treatment raise the question of whether the delayed therapeutic influence of TCAs and ECS may reflect the development of a time dependent sensitization process. If so, it suggests the possibility that daily TCA or frequent ECS may not be necessary to obtain (and/or maintain) therapeutic efffects. 6 references. (Author abstract modified)

002660 Aronstam, Robert S. Dept. of Pharmacology, Medical College of Georgia, Augusta, GA 30912 **Interactions of tricyclic antidepressants with a synaptic ion channel.** Life Sciences. 28(1):59-64, 1981.

The interactions of four tricyclic antidepressants, including two dibenzazepines (imipramine and desipramine), and two dibenzocycloheptenes (amitriptyline and nortryptiline), were studied with the ion channel associated with the nicotinic aceytlcholine receptor from the electric organs of Torpedo ocellata. These drugs inhibited the binding of tritiated perhydrohistrionicotoxin and phencyclidine to sites on the ion channel. All four compounds interacted with the ion channel with approximately equal affinities, inhibition constants for the two sites ranging from 1.1 to 3.4 mcM in the absence, and from 0.1 to 0.75 mcM in the presence of 1 mcM acetylcholine. The affinities of the secondary amines were increased by acetylcholine to a greater degree than were those of the tertiary amine compounds. 14 references. (Author abstract)

002661 Ayala-Guerrero, F.; Perera-Ortiz, Y.; Vargas, L. Depto. de Neurobiologia, Instituto de Investigaciones Biomedicas, UNAM, Ciudad Universitaria, Mexico 20 DF, Mexico **Phasic activity induced by p-chlorophenylalanine in the auditory pathway.** Neuropharmacology. 20(3):273-275, 1981.

Intraperitoneal injections of p-chlorophenylalanine (PCPA) induced phasic activity in structures of the auditory pathway (cochlear nucleus and auditory cortex) and visual pathway (lateral geniculate body and visual cortex) of cats. Total insomnia was observed 48 to 72 hours after injection of the drug. Similar activity has been observed in other brain structures after administration of PCPA or reserpine and during paradoxical sleep. 18 references. (Author abstract modified)

002662 Bacopoulos, N. G; Roth, R. H. Dept. of Pharmacology, Dartmouth Medical School, Hanover, NH 03755 **Apomorphine-haloperidol interactions: different types of antagonism in cortical and subcortical brain regions.** Brain Research. 205(2):313-319, 1981.

Apomorphine, a dopamine (DA) receptor stimulant, was found to induce a dose dependent decrease in the content of the dopamine metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in the olfactory tubercle and striatum of rats, but was ineffective in the frontal cortex. Apomorphine also antagonized the haloperidol induced accumulation of DOPAC and HVA in the olfactory tubercle and striatum, whereas in the frontal cortex it antagonized the effects of haloperidol on DOPAC but not on HVA. THe total (free and conjugated) content of DA metabolites was measured in these studies. 17 references. (Author abstract modified)

002663 Baklavadzhyan, O. G.; Darbinyan, A. G.; Gekht, K; Poppay, M.; Taturyan, I. Kh.; Antonyan, M. N. Lab. fiziologii vegetativnoy nervnoy sistemy Instituta fiziologii im. L. A. Orbeli Akademii nauk Arm SSR, Yerevan, USSR **/Self-stimulation reaction in normotensive and hypertensive rats./** Reaktsiya samorazdrazheniya u normotenzivnykh i gipertenzivnykh krys. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 30(6):1187-1195, 1980.

Self-stimulation in normotensive and hypertensive rats was studied in 16 male rats in relation to the part of noradrenergic mechanisms in self-stimulation operant behavior. Small doses of noradrenaline facilitated self-stimulation, while high doses depressed or stopped it. The depressive effect was accompanied by a marked increase of systolic blood pressure. Effective blockade of beta-adrenoceptive structures by Inderal suppressed systolic blood presure, and the inhibitory effect was accompanied by a small decrease of systolic blood pressure. The suppressing effect of the alpha-adrenoblocking agent, phentolamine, was even more pronounced, but was accompanied by a marked decrease of systolic blood pressure. Beta-agonist Isadrin facilitated self-stimulation without changing systolic blood pressure. Results suggest that positive reward in the lateral hypothalamus is due to a direct stimulation of beta-adrenoceptive noradrenergic neuronal elements, and that reduction of lever-pressing rate during acute and chronic neurogenic hypertension is related to baroreceptor mechanisms. 30 references. (Journal abstract modified)

002664 Balldin, Jan; Bolle, Paula; Eden, Staffan; Eriksson, Elias; Modigh, Kjell. Psychiatric Research Centre, St. Jorgen's Hospital, S-422 03 HISINGS BACKA, Sweden **Effects of electroconvulsive treatment on growth hormone secretion induced by monoamine receptor agonists in reserpine-pretreated rats.** Psychoneuroendocrinology. 5(4):329-337, 1980.

The effects of electroconvulsive treatment (ECT) on growth hormone (GH) secretion induced by monoamine receptor agonists in reserpine treated rats were investigated. ECT was administered to rats with implanted intraaortic cannulae as one electroconvulsion (ECS) daily for 7 days. ECT pretreated and control rats received identical drug treatments (pretreatment with reserpine and then clonidine, apomorphine, MK-486, or 5-hydroxytryptophan). Combined treatment with clonidine and MK-486 plus 5-hydroxytryptophan induced a more pronounced GH secretion than administration of clonidine alone in both ECT pretreated and in control animals. The response was significantly weaker in the ECT pretreated Ss than in the control animals. Results are in accord with the contentions that ECT changes the responsiveness of postsynaptic receptors sensitive to DA or 5-HT, or neutral structures connected to such receptors. Moreover, they support the view that NA neurons have a fundamental role in the regulation of GH secretion in rats. 30 references. (Author abstract modified)

002665 Barker, Jeffery L.; Mathers, David A. Laboratory of Neurophysiology, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20205 **GABA analogues activate channels of different duration on cultured mouse spinal neurons.** Science. 212(4492):358-361, 1981.

Voltage clamp recordings from mouse spinal neurons grown in culture were used to study the membrane current fluctuations induced by 12 substances that are structurally similar to gamma-aminobutyric acid (GABA). Fluctuation analysis provided estimates of the electrical properties of the elementary events underlying these responses. Estimates of the mean conductance of channels activated by all of the substances, except glycine, did not differ significantly from that estimated for GABA, whereas mean durations of agonist activated channels all differed significantly from that found for GABA. The results indicate that all of the substances tested, except glycine, activate channels of similar conductance but of different durations. 13 references. (Author abstract modified)

002666 Barker, Jeffery L.; Mathers, David A. Laboratory of Neurophysiology, NINCDS, Bethesda, MD 20205 **GABA receptors and the depressant action of pentobarbital.** Trends in NeuroSciences. 4(1):10-13, 1981.

The research literature concerning GABA receptors and the depressant action of pentobarbital is reviewed, and the question of whether the GABAmimetic effects of pentobarbital involve GABA receptors is considered. Pentobarbital has a variety of cellular actions which would be expected to contribute to depression of CNS excitability. It appears to be able to activate Cl- ion channel like mechanisms in the membrane of CNS neurons possibly through engagement of receptor like sites. Although the elementary signal evoked by the drug has the same amplitude as that activated by GABA and although the drug effect can be antagonized by agents which block GABA responses, it cannot be concluded that the drug activates a GABA receptor coupled Cl- ion conductance. A second action of the barbiturates involves potentiation of GABA responses and this modulatory action also shows some stereospecific requirements. 15 references. (Author abstract modified)

002667 Bartfai, T.; Hedlund, B.; Jarv, J.; Nordstrom, O. Dept. of Biochemistry, Arrhenius Laboratory, S-106 91 Stockholm, Sweden **Muscarinic acetylcholine receptor. (Unpublished paper).** Research Report, NIMH Grant, MH-31107, 1979. 6 p.

Muscarinic acetylcholine receptors from rat cerebral cortex and small intestine were studied by the high affinity and high specific activity antagonists 3H-3-quinuclinidyl benzilate (3-QNB) and 3H-N-methyl-4-piperidinyl benzilate (4-NMPB). A reaction sequence is described, based on equilibrium binding data and studies on association and dissociation rates of the receptor antagonist complex. Results of agonist binding studies carried out under equilibrium conditions can be described as if there were two classes of agonist binding sites with affinities 100mM and 0.05mcM for carbamylcholine. It appears that it is the low affinity binding site that is associated with muscarinic activation of cyclic GMP synthesis in cortical slices and in N1E 115 neuroblastoma cells. Experiments with the cardiotoxin from N. m. mossambica, indicate that the cardiotoxin and D600 may share some common site on the receptor coupled Ca2 channel, or on the muscarinic receptor itself. 11 references. (Author abstract modified)

002668 Becker, Jill B.; Ramirez, V. D. Ramirez: Dept. of Physiology and Biophysics, 524 Burrill Hall, University of Illinois, Urbana, IL 61801 **Sex differences in the amphetamine stimulated release of catecholamines from rat striatal tissue in vitro.** Brain Research. 204(2):361-372, 1981.

Sex and estrous cycle related differences in the amphetamine (AMT) stimulated release of catecholamines (CA) from rat striatal and mediobasal hypothalamus (MBH) fragments were measured in an in vitro perifusion system. In striatal tissue from intact males, AMT stimulated the release of both norepinephrine (NE) and dopamine (DA). The AMT stimulated release of DA from striatal tissue obtained from intact females varied with the stage of the estrous cycle. This increase in DA release was lower in striatal tissue from proestrous females than from females in estrus or diestrus. MBH fragments from intact or gonadectomized rats, with or without hormonal treatment, demonstrated a consistent AMT stimulated release of DA, regardless of the sex of the animal. The AMT stimulated NE release from these MBH fragments was less consistent, but there were not significant differences between the groups. These results demonstrate that the AMT stimulated release of DA from striatal tissue in vitro is sex, hormonal, and tissue dependent. 39 references. (Author abstract modified)

002669 Bergey, G. K.; Fitzgerald, S. C.; Schrier, B. K.; Nelson, P. G. Laboratory of Developmental Neurobiology, NIH, Bethesda, MD **Neuronal maturation in mammalian cell culture is dependent on spontaneous electrical activity.** Brain Research. 207(1):49-58, 1981.

The role of electrical activity in the maturational process observed in fetal mouse spinal cord (SC) and dorsal root ganglion (DRG) cultures was investigated with tetrodotoxin (TTX), the specific blocker of the voltage sensitive sodium channel responsible for action potential generation. This agent completely eliminates the spikes and related synaptic activity which occur abundantly in untreated cultures. Such blockade of electrical activity in the cultures, when begun early (day 1 or day 8 in vitro), results in a 85% to 95% reduction in the number of large SC neurons, without affecting DRG neuron numbers. TTX treatment initiated when cultures are mature (day 70) has no significant effect on either DRG or SC neurons. Intermediate effects are obtained when treatment is initiated at day 35 in vitro. The activity of the nerve specific enzyme, choline acetyltransferase, is decreased significantly by early TTX treatment, while DNA and protein content of the cultures (primarily contributed by glial and fibroblastic cells) is not affected. 31 references. (Author abstract modified)

002670 Bevan, John A. Dept. of Pharmacology, UCLA School of Medicine, Center for Health Sciences, Los Angeles, CA 90024 **A comparison of the contractile responses of the rabbit basilar and pulmonary arteries to sympathomimetic agonists: characteristics.** Journal of Pharmacology and Experimental Therapeutics. 216(1):83-89, 1981.

The characteristics of the alpha-adrenoceptor mediated contractile responses of isolated rabbit basilar and pulmonary arteries to a series of phenethylamines and imidazolines have been compared. Vascular segments from normal and chronically reserpinized rabbits, pretreated in the tissue bath with desmethylimipramine and propranolol and propranolol pretreated segments from chronically denervated basilar arteries were used. The responses of the basilar artery to a series of amines mediated by alpha-adrenoceptors show properties both similar to and different from those of the pulmonary artery. Although the basilar artery is less sensitive and has a peak response less than that of which the tissue is capable, many features of the responses of the two arteries to phenethylamine like compounds are similar. However, the basdilar artery, unlike the pulmonary artery, does not contract in response to imidazoline derivatives. This latter feature has been observed in some other smaller peripheral vessels. 39 references. (Author abstract modified)

002671 Bignami, Giorgio. Istituto Superiore di Sanita, Viale Regina Elena 299, I-00161 Roma, Italy **Pharmacological evidence on the specialization of CNS mechanisms responsible for motor act inhibition by aversive events.** Acta Neurobiologiae Experimentalis. 39(6):395-412, 1979.

Psychopharmacological studies of CNS mechanisms subserving the inhibition of motor acts by aversive events are described. Studies using a go/no go paradigm indicate that perseverative deficits and impairment of sensory processes may be inseparable. The complex profile of cue dependent disinhibitory effects of antimuscarinic agents suggests that separate sensorimotor mechanisms are employed for response suppression not simply as a function of cue type, response type, or response/reinforcement relations, but as a joint function of all these factors. Sedative/tranquilizing agents with anticonflict properties are maximally effective in disrupting response withholding when both reward and punishment follow the emission of a particular response, are less consistently effective in tests with CS paired with noncontingent shock, and are mostly ineffective in those go/no go avoidance tasks which show high sensitivity to muscarinic blockade. 48 references. (Author abstract modified)

002672 Biswas, B.; Jonsson, G. Jonsson: Dept. of Histology, Karolinska Institutet, S-104 01 Stockholm, Sweden **Reversal of noradrenaline denervation-induced increase of beta-adrenoreceptor binding in rat neocortex by noradrenaline infusion.** European Journal of Pharmacology. 69(3):341-346, 1981.

The effect of intraventricular infusion of (-)-noradrenaline (NA) on beta-receptor (3H-dihydroalprenolol) binding in the cerebral cortex was studied in male Sprague-Dawley rats treated with 6-hydroxydopamine (6-OHDA) or saline shortly after birth. When these animals were 8 to 10 weeks old, the NA level in the cerebral cortex of 6-OHDA treated rats was only 70 to 80% of the control level. Vehicle infusion did not alter beta-adrenoceptor binding in the control animals, but increased binding by 30 to 50% 6-OHDA treated animals. This increase was counteracted by infusion of NA. NA did not alter beta-adrenoceptor binding in control rats when infused at 1mcg/hour, but decreased binding by 24% when infused at 5mcg/hour. Results suggest that the availability of NA at receptor sites regulates the density of beta-adrenoceptor binding and may thereby regulate the NA sensitivity of cells with beta-receptors. 11 references. (Author abstract modified)

002673 Bloxam, D. L.; Tricklebank, M. D.; Patel, A. J.; Curzon, G. Curzon: Dept. of Neurochemistry, Institute of Neurology, MRC Developmental Neurobiology Unit, London WC1N 2NS, England **Effects of albumin, amino acids, and clofibrate on the uptake of tryptophan by the rat brain.** Journal of Neurochemistry. 34(1):43-49, 1980.

Tryptophan uptake into male Sprague-Dawley rat forebrain was substantially influenced by albumin binding and competition from other amino acids, but hypothalamic uptake was less influenced by these factors. When free tryptophan was doubled but total tryptophan was unchanged, uptake was increased by 53% into forebrain and by 28% into hypothalamus. When plasma total tryptophan concentration was decreased by 45% but free tryptophan and competing amino acid concentrations were unchanged, uptake was unchanged. 29 references. (Author abstract modified)

002674 Blume, H. W.; Pittman, Q. J.; Renaud, L. P. Renaud: Division of Neurology, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada **Sensitivity of identified medial hypothalamic neurons to GABA, glycine and related amino acids; influence of bicuculline, picrotoxin and strychnine on synaptic inhibition.** Brain Research. 209(1):145-158, 1981.

Medial hypothalamic neurons in pentobarbital anesthetized rats were identified by location and response to electrical stimulation of the amygdala, medial preoptic area, midbrain periaqueductal gray, and median eminence. Cells were then examined for their sensitivity to microiontophoretic applications of GABA, glycine and three related amino acids, i.e. beta-guanidinopropionic acid, delta-aminovaleric acid, and beta-alanine. Application of all agents decreased the spontaneous and glutamate or aspartate evoked activity of the majority of neurons in all identified categories. The majority of neurons were more sensitive to beta-guanidinopropionate, delta-aminovalerate, GABA than to glycine and beta-alanine. Bicuculline and picrotoxin produced a selective and reversible antagonism of depressions evoked by GABA and GABA like amino acids whereas strychnine produced a selective and reversible antagonism of depressions evoked by glycine and beta-alanine. These observations suggest that many medial hypothalamic neurons have both GABA and glycine receptors but that GABA may have the more important role as a neurotansmitter common to afferent or recurrent inhibitory hypothalamic pathways. 41 references. (Author abstract modified)

002675 Bornheim, Lester M.; Borys, Henry K.; Karler, Ralph. Karler: Dept. of Pharmacology, 2C 202 Medical Center, University of Utah College of Medicine, Salt Lake City, UT 84132 **Effect of cannabidiol on cytochrome P-450 and hexobarbital sleep time.** Biochemical Pharmacology. 30(5):503-507, 1981.

The influences of acute and subacute cannabidiol (CBD) treatment and of subsequent drug withdrawal were investigated on hexobarbital induced sleep time, on hepatic cytochrome P-450 concentration, on the in vitro formation of carbon monoxide (CO) associated with CBD metabolism, and on the kinetics of aminopyrine N-demethylase metabolism. In acutely treated mice, CBD prolonged sleep time, decreased cytochrome P-450 concentration, decreased the endogenous formation of CO, and increased an apparent Km for aminopyrine N-demethylase activity. In subacutely treated animals, tolerance developed to the effect on sleep time but not to that on cytochrome P-450 concentration nor on the endogenous formation of CO in vitro nor on the Km for the N-demethylase activity. Results support the conclusion that the CBD effect on sleep time is not correlated with either total amount of cytochrome P-450 or with the CBD depressant effect on the cytochrome. 20 references. (Author abstract modified)

002676 Braestrup, Claus; Nielsen, Mogens; Skovbjerg, Hanne; Gredal, Ole. Research Laboratories, A/S Ferrosan, 5 Sydmarken, DK-2860 Soeborg, Denmark **Beta-carboline-3-carboxylates and benzodiazepine receptors.** Advances in Biochemical Psychopharmacology. 26:147-155, 1981.

Studies of beta-carboline-3-carboxylate (beta-CCE), a compound obtained from human urine, which indicate that beta-CCE may be an exogenous ligand for benzodiazepine receptors, are described. Results suggest that tritium labelled propyl beta-carboline-3-carboxylate may be a selective ligand for subclasses of benzodiazepine receptors, in particular the P51 molecular species (cerebellar type) demonstrated by Sieghart and Karobath. Alternatively, true negative cooperativity may exist in the hippocapus and the findings of complexes with a molecular weight of 110,000 daltons may be relevant to the molecular arrangements responsible for these proposed site to site interactions. 31 references.

002677 Brandt, M.; Buchen, C.; Hamprecht, B. Hamprecht: Physiologisch-chemisches Institut des Universitat, Koellikerstr 2, D-8700, Wurzburg, West Germany **Relationship between the actions of calcium ions, opioids, and prostaglandin E1 on the level of cyclic AMP in neuroblastoma X glioma hybrid cells.** Journal of Neurochemistry. 34(3):643-651, 1980.

The influence of calcium ions (Ca2) on the increase in cyclic AMP induced by prostaglandin-E1 (PGE1) in neuroblastoma/glioma hybrid cells and the antagonism of this effect by opioids was studied. The increase in intracellular cyclic AMP induced by PGE1 was strongly dependent on Ca2, but the inhibitory effect of leucine-enkephalin was not Ca2 dependent. Cells exposed to opioids or Ca2 deficiency in short-term experiments had lowered levels of cyclic AMP. In long-term experiments, exposure to opioids or to Ca2 deficiency caused an increased maximal response to PGE1. 52 references. (Author abstract modified)

002678 Brennan, M. J. W.; Cantrill, R. C.; Krogsgaard-Larsen, P. Brain Research Group, Dept. of Medical Biochemistry, School of Pathology, University of the Witwatersrand, Johannesburg 2001, South Africa **GABA autoreceptors: structure-activity relationships for agonists.** Advances in Biochemical Psychopharmacology. 26:157-167, 1981.

The potency of a number of GABA agonists in inhibiting K stimulated release of 3H-GABA from preloaded rat cortical synaptosomes was investigated and compared with the potency of the drugs in inhibiting specific 3H binding to cortical synaptic plasma membranes. Pharmacological differences between the autoreceptors and the sites labelled with 3H-GABA were analyzed. Data suggest that the GABA autoreceptors and the receptors labelled by 3H-GABA in synaptic membranes show considerable pharmacological similarity. Results provide the first direct correlation between a GABA receptor mediated effect and receptor occupancy. It appears that the autoreceptor is coupled directly to the effector mechanism (presumably a chloride channel) and that there are no spare autoreceptors on the presynaptic terminal. Results suggest that the autoreceptors are distinct from bicuculline insensitive presynaptic GABA receptors and more closely resemble the classical postsynaptic GABA binding site. 35 references.

002679 Briggs, Roger S.; Redgrave, Peter; Nahorski, Stefan R. Dept. of Pharmacology and Therapeutics, Medical Sciences Building, University of Leicester, University Road, Leicester LE1 7RH **Effect of kainic acid lesions on muscarinic agonist receptor subtypes in rat striatum.** Brain Research. 206(2):451-456, 1981.

The neurotoxin kainic acid was employed to attempt to demonstrate a differential cellular localization of muscarinic agonist binding sites in the corpus striatum. Identical proportions of high affinity and low affinity muscarinic agonist sites were observed in kainate lesioned striatum, despite a substantial loss of total muscarinic receptors. Results confirm previous data and suggest that a substantial proportion of striatal muscarinic sites are present on striatal perikarya. Results also suggest that identical proportions of high and low affinity agonist sites are present on striatal cell bodies and on structures (glia, blood vessels, nerve terminals, axons of passage, and surviving cell bodies) remaining after kainate lesions. It is suggested that the separate noninteracting muscarinic agonist sites in brain can occur on the same cell type. 13 references. (Author abstract modified)

002680 Browder, Sally; German, Dwight C.; Shore, Parkhurst A. Dept. of Psychiatry, University of Texas Health Science Center, Dallas, TX 75235 **Midbrain dopamine neurons: differential responses to amphetamine isomers.** Brain Research. 207(2):333-342, 1981.

Responses of midbrain dopamine neurons to amphetamine isomers were investigated. Intravenously administered D-amphetamine and L-amphetamine have different potency ratios in reducing the firing rates of dopamine cells in the substantia nigra and in the ventral tegmental area. While D-amphetamine is considerably more potent than L-amphetamine in reducing ventral substantia nigra dopamine neuronal impulse flow, D and L isomers are of similar potency in reducing dorsal substantia nigra and ventral tegmental dopamine neuronal impulse flow. These results suggest that all dopamine cell groups are not pharmacologically identical and that different dopamine nuclei may respond differently to psychoactive drugs. The comparable potencies of the D and L isomers on dorsal substantia nigra and ventral tegmental area dopamine neurons may explain, by a dopamine mechanism, the finding that comparable doses of the isomers produce schizophrenia like symptoms. 60 references. (Author abstract modified)

002681 Broxterman, Henk J.; Noach, Erik L.; van Valkenburg, Cees F. M.; Wijling, Amerentia. Leiden University Medical Centre, Dept. of Pharmacology, Wassenaarseweg 72, NL-2333 AL Leiden, The Netherlands **Cross-tolerance of dopamine metabolism to baclofen, gamma-butyrolactone and HA-966 in the striatum and olfactory tubercle of the rat.** Life Sciences. 28(9):973-981, 1981.

Cross-tolerance of dopamine (DA) metabolism to baclofen, gamma-butyrolactone (GBL) and HA-966 in the striatum and olfactory tubercle (OT) of the rat is described. Rats received 7 daily injections of one substance or the other. Marked tolerance and cross-tolerance for the DA elevating effect of these drugs was observed in striatum, but not in OT. On day 7, the nigrostriatal pathway was unilaterally lesioned, and some tolerance to the DA increase in the striatum on the lesioned side was observed in HA-966 pretreated rats. However, this tolerance was small compared to the tolerance after an additional drug administration in nonlesioned animals. Results show that the tolerance develops to the increase of DA synthesis, and that this increase is possibly receptor mediated. This tolerance develops more readily in the striatum than in the olfactory tubercle. 34 references. (Author abstract modified)

002682 Bruni, A.; Bigon, E.; Cappellazzo, G.; Boarato, E.; Leon, A.; Toffano, G. Institute of Pharmacology, University of Padova, Padova, Italy **Physiologic and pharmacologic implications in the deacylation of phosphatidylserine in mice.** In: Amaducci, L., Aging of the brain and dementia, vol. 13. New York, Raven, 1980. 326 p. (p. 119-122).

Research on the physiological and pharmacological implications of the deacylation of phosphatidylserine in mice is reviewed, with emphasis on the influence of lysophosphatidylserine (LPS) on brain energy metabolism. This research demonstrates the ability of LPS to promote the release of amines stored in specialized cells. Specifically, LPS, in combination with endogenous factors (as yet detected only in mouse plasma), triggers the release of amines from intracellular stores with subsequent catecholamine efflux from the adrenals and hyperglycemia. A similar event in the brain may lead to reduced neuronal activity and to glucose accumulation. The possibility of LPS formation in tissues and the minute amount needed for activity indicate that LPS deserves attention as an autocoid compound in vivo. 9 references.

002683 Budek, Michael; Barkai, Amiram I.; Brown, David L.; Fieve, Ronald R. Barkai: New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Suppression of amphetamine-induced EEG arousal in the hippocampus of haloperidol-treated rabbits.** Neuropsychobiology. 7(2):99-104, 1981.

Changes of hippocampal EEG activity resulting from administration of d-amphetamine were investigated in rabbits before, during, and after chronic treatment with haloperidol. Cross-zero analysis of EEG data showed that chronic treatment with haloperidol attenuated the amphetamine induced increase in hippocampal theta rhythm. The increase of theta activity by amphetamine was fully restored 39 days after withdrawal of haloperidol. Further, haloperidol reduced the incidence of spontaneous theta rhythm in three of four animals. It is suggested that the enhancement of hippocampal theta by d-amphetamine is mediated in part by dopaminergic mechanisms which are susceptible to the action of haloperidol. 25 references. (Author abstract modified)

002684 Burchfiel, James L.; Duffy, Frank H. Seizure Unit, Children's Hospital Medical Center, Boston, MA 02115 **Role of intracortical inhibition in deprivation amblyopia: reversal by microiontophoretic bicuculline.** Brain Research. 206(2):479-484, 1981.

The role of intracortical inhibition in deprivation amblyopia and its reversal by microiontophoretic bicuculline were investigated. The GABA antagonist, bicuculline, was microiontophoretically applied to 31 cells in the visual cortices of four cats monocularly deprived of vision from birth to time of study at age 5 months. Bicuculline restored input from the deprived eye to 42% of cells studied. Elevation background firing rates by glutamate failed to restore deprived eye input. It is suggested that intracortical inhibition plays an important role in maintaining the physiological abnormalities produced in visual cortex by monocular deprivation. 22 references. (Author abstract modified)

002685 Burrows, G. Howard; Myers, Michael M.; Whittemore, Scott R.; Hendley, Edith D. Dept. of Obstetrics and Gynecology, Southwestern Medical School, 5323 Harry Hines Blvd., Dallas, TX 75235 **Calcium-sensitive accumulation of norepinephrine in rat cerebral cortex.** European Journal of Pharmacology. 69(3):301-312, 1981.

The accumulation of (3H) l-norepinephrine (3H-NE) was studied in a crude synaptosomal preparation of male Sprague-Dawley rat cerebral cortex. When sodium dependent, high affinity, saturable transport (uptake-1) was blocked, 3H-NE accumulation showed rapid initial rates and was inhibited by metaraminol but not by normetanephrine. This accumulation was calcium sensitive and appeared to be localized in nerve endings. At high concentrations of 3H-NE and short incubation times, calcium sensitive accumulation accounted for most of the total accumulation of 3H-NE; uptake-1 contributed only a small portion. Results suggest that calcium sensitive accumulation may be a significant factor for noradrenergic transmission. 36 references. (Author abstract modified)

002686 Chakravarty, Indira; Ghosh, J. J. All India Institute of Hygiene and Public Health, Government of India, 110, Chittaranjan Avenue, Calcutta 700 073 India **Influence of cannabis and delta9-tetrahydrocannabinol on the biochemistry of the male reproductive organs.** Biochemical Pharmacology. 30(4):273-276, 1981.

The effects of repeated subcutaneous administration of cannabis extract and delta9-tetrahydrocannabinol (THC) on the fructose and citric acid contents of male reproductive organs of prepubertal as well as adult albino rats were studied. Results indicate that both the fructose and the citric acid contents of the male reproductive organs are reduced significantly by cannabis. The reduction further appears to be related to the amount of THC being administered in both young and adult rats. Results corroborate previously reported antitestosteronic action of the drug. 20 references. (Author abstract modified)

002687 Chapin, John K.; Waterhouse, Barry D.; Woodward, Donald J. Dept. of Cell Biology, University of Texas Health Science Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75235 **Differences in cutaneous sensory response properties of single somatosensory cortical neurons in awake and halothane anesthetized rats.** Brain Research Bulletin. 6(1):63-70, 1981.

The effect of halothane anesthesia on different latency components of cutaneous sensory responses of single units in the primary somatosensory (SI) cortex of rats was investigated. Quantitative studies of computer generated poststimulus time histograms were used to determine whether the increase in nonspecific properties often observed in the SI cortices of awake animals were attributable to a generally increased sensory responsiveness of these cells or to a selective increase of certain nonspecific components of their sensory response. Sensory specificity was investigated by measuring the size of cutaneous receptive fields of single cells and testing their ability to follow high stimulus frequencies. It is concluded that although halothane anesthesia slightly depressed the short latency response component (E1a) exhibiting highly specific sensory properties, its main effect was to depress the longer latency excitatory components (E1b and E2) which exhibited relatively nonspecific properties. 23 references. (Author abstract modified)

002688 Childers, Steven R.; Snyder, Solomon H. Snyder: Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Differential regulation by guanine nucleotides of opiate agonist and antagonist receptor interactions.** Journal of Neurochemistry. 34(3):583-593, 1980.

Guanosine triphosphate (GTP) had no effect on the binding of tritiated opiate antagonists to male Sprague-Dawley rat brain membranes in the presence of 100mM sodium chloride, but decreased labeled opiate agonist binding by 60 to 95%. In the absence of sodium, GTP decreased binding of agonists by 20 to 60% and that of antagonists by 0 to 20%. Guanosine monophosphate was less potent than GTP or guanosine diphosphate in decreasing agonist binding. GTP increased the association rate of (3H)dihydromorphine twofold and increased the dissociation rate fourfold, but had no efect on the association or dissociation rates of (3H)diprenorphine. The affinities of antagonists in inhibiting (3H)diprenorphine binding were not affected by GTP or sodium, but the affinities of agonists were reduced 40 to 120-fold. Divalent cations, especially manganese, reversed the effects of GTP on agonist binding by stimulating membrane bound phosphatases. It is suggested that GTP, through its selective effect on agonist binding, may regulate opiate receptor interactions with their physiological effectors. 32 references. (Author abstract modified)

002689 Chu, Nai-Shin. Dept. of Neurology, University of California, Irvine Medical Center, 101 City Drive South, Orange, CA 92668 **Caffeine- and aminophylline-induced seizures.** Epilepsia. 22(1):85-94, 1981.

The epileptogenicity of caffeine and aminophylline was studied in rats. Intraperitoneal administration of caffeine produced an immediate excitation and seizures followed by an encephalopathy. A progression from encephalopathy to seizures was observed following aminophylline administration. During the development of behavioral sezures, the EEGs showed a progression from fast activity isolated or bursts of spikes and/or sharp waves to full blown epileptiform discharges. A wide spectrum of cardiac arrhythmias was observed during and following the seizures. Epileptiform activities ranging from isolated or burst of spikes and/or sharp waves to continuous epileptiform discharges were observed following local application of the drugs to the cerebral cortex. 28 references. (Author abstract modified)

002690 Cocchi, D.; Casanueva, F.; Locatelli, V.; Apud, J.; Martinez-Campos, A.; Civati, C.; Racagni, G.; Muller, E. E. Dept. of Pharmacology, University of Milan, I-20129 Milan, Italy **Gabaergic mechanisms in the control of PRL and GH release.** Advances in Biochemical Psychopharmacology. 26:247-259, 1981.

Data concerning the mechanisms subserving the central stimulatory and peripheral inhibitory components of GABA action on prolactin (PRL) release and the action of the GABAergic system on the control of growth hormone (GH) secretion are presented. Use of the specific peripheral GABA antagonist bicuculline methiodide (BIC Met I-) blocked the inhibition of PRL release induced by systemic administration of muscimol, thus providing in vivo evidence that peripheral GABA receptors play a major role in this endocrine response. Failure of Bic Met I- to counteract the initial muscimol induced PRL rise substantiates the view that the latter is due to activation of central GABA receptor sites. Preliminary experiments on the involvement of the GABAergic mechanisms in the control of GH secretion suggest that, similar to PRL control, there exists a peripheral inhibitory component (pituitary) in addition to a central GABAergic component stimulatory to GH release. 36 references.

002691 Collingridge, G. L.; Collins, G. G. S.; Davies, J.; James, T. A.; Neal, M. J.; Tongroach, P. School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Effect of tentanus toxin on transmitter release from the substantia nigra and striatum in vitro.** Journal of Neurochemistry. 34(3):540-547, 1980.

The effects of tetanus toxin on the uptake and release of radiolabeled transmitters from slices of male rat substantia nigra (SN) and striatum were studied. Injection of tetanus toxin into the SN 6 hours before slice preparation significantly reduced the calcium dependent, potassium evoked release of (3H)GABA, but did not alter endogenous GABA level or (3H)GABA uptake in the SN. Injections of tetanus toxin into the striatum significantly reduced the calcium dependent, potassium evoked release of (14C)GABA and (3H)dopamine, but had no effect on potassium evoked release of (3H)5-hydroxytryptamine or (14C)acetylcholine. It is concluded that tetanus toxin inhibits GABA release directly rather than by interfering with synthesis or inactivation processes. 29 references. (Author abstract modified)

002692 Connors, Barry W. Dept. of Neurology, Stanford University School of Medicine, Stanford, CA 94305 **A comparison of the effects of pentobarbital and diphenylhydantoin on the GABA sensitivity and excitability of adult sensory ganglion cells.** Brain Research. 207(2):357-369, 1981.

The actions of pentobarbital (PB) and diphenylhydantoin (DPH) on neurons of dorsal root ganglia of adult rats were studied. At anesthetic levels, PB greatly enhanced neuronal responses to GABA. At somewhat higher concentrations, PB caused a small depolarization and profoundly attenuated GABA responses, probably because of cross-desensitization of GABA receptors. In contrast to results in some nonmammalian species, DPH did not affect GABA responses under any conditions. PB depressed single intracellularly evoked action potentials only at high concentrations, but the cell's ability to fire trains of impulses in response to prolonged depolarization was impaired at anesthetic dosage level. Results suggest that the anesthetic properties of PB may depend, in part, on the enhancement of GABA mediated inhibitions and increased accomodation. The anticonvulsant DPH exerts a selective, tetrodotoxin like depression of sodium conductances which does not extend to sodium conductances which are insensitive to tetrodotoxin. 45 references. (Author abstract modified)

002693 Crowley, William R.; Terry, L. Cass. Dept. of Pharmacology, University of Tennessee, Center for the Health Sciences, Memphis, TN 38163 **Effects of an epinephrine synthesis inhibitor, SKF64139, on the secretion of luteinizing hormone in ovariectomized female rats.** Brain Research. 204(1):231-235, 1981.

To test the involvement of central epinephrine systems in luteinizing hormone (LH) secretion, the epinephrine synthesis inhibitor, SKF64139, was administered to ovariectomized rats treated with ovarian hormones. This agent significantly decreased resting LH concentrations in ovariectomized, hormonally untreated rats and completely suppressed the stimulatory feedback effects of estrogen plus progesterone. In these animals, hypothalamic concentrations of epinephrine, but not norepinephrine or dopamine, were significantly decreased. It is suggested that brain epinephrine may participate in the neural control of LH secretion in rats. 21 references. (Author abstract)

002694 Cuche, H. 1, rue Cabanis, F-75674 Paris Cedex, France **/How antidepressant drugs act./** Mecanismes d'action des antidepresseurs. Evolution Psychiatrique. 45(4):767-774, 1980.

The main ways in which antidepressant drugs act at the synaptic level are discussed. It is emphasized that data at present are fragmentary and that there is, consequently, a danger of oversimplification. However, in order to use antidepressants effectively in therapeutic practice, it appears necessary to understand how they act, so that the most appropriate antidepressant is chosen. The therapist is warned against choosing an antidepressant on the basis of habit. (Journal abstract modified)

002695 Dalterio, S. L.; Michael, S. D.; Macmillan, B. T.; Bartke, A. Dept. of Pharmacology, University of Texas Health Science Center at San Antonio, San Antonio, TX 78284 **Differential effects of cannabinoid exposure and stress on plasma prolactin, growth hormone and corticosterone levels in male mice.** Life Sciences. 28(7):761-766, 1981.

The differential effects of cannabinoid exposure and stress on plasma prolactin (PRL), growth hormone (GH), and corticosterone levels in male mice were investigated. Plasma PRL levels were reduced in stressed and nonstressed male mice after a single dose of delta9-tetrahydrocannabinol (THC), while GH levels were reduced only in nonstressed animals. Chronic treatment with THC did not affect PRL or GH levels under either condition. Neither acute nor repeated exposure to THC affected plasma conticosterone levels. In contrast to the effects of THC, acute exposure to cannabinol (CBN) increased plasma GH levels in nonstressed mice, while repeated CBN treatments reduced GH levels in stressed animals. Moreover, chronic CBN exposure resulted in decreased peripheral levels of corticosterone in both stressed and nonstressed mice, and reduced plasma PRL levels in stressed mice. Thus, psychoactive and nonpsychoactive components of marihuana can exert different effects on endocrine function and on responsivity to stress in male mice. 26 references. (Author abstract modified)

002696 Davies, J.; Watkins, J. C. Dept. of Pharmacology, School of Pharmacy, London WC1N 1AX, England **Differentiation of kainate and quisqualate receptors in the cat spinal cord by selective antagonisms with gamma-D(and L)-glutamylglycine.** Brain Research. 206(1):172-177, 1981.

The effects on cat spinal neurons of the D-isomer and L-isomer of gamma-glutamylglycine (gamma-DGG and gamma-LGG), which have been shown to differenitally depress responses to excitatory amino acids in the frog spinal cord, were investigated. Gamma-DGG and gamma-LGG were found to depress N-methyl-D-aspartate (NMDA) induced excitation, L-aspartate induced excitation, and kainate induced excitation in cat spinal cord while having little or no effect on L-glutamate induced responses or quisqualate induced responses. The dipeptides also depress dorsal root evoked exicitation of Renshaw cells, but not acetylcholine evoked or ventral root evoked excitation of these cells. The D-form of the dipeptide is more potent than the L-form. Results are interpreted in favor of three types of receptors for excitatory amino acids on spina neurons, these being sensitive to the selective agonist action of NMDA, kainate, and quisqualate. 29 references. (Author abstract modified)

002697 Davis, Jesse C.; Bigger, J. Thomas, Jr. Bigger: Dept. of Medicine, Columbia University, 630 W. 168th St., New York, NY 10032 **The effects of thioridazine on electrical and ischemic ventricular fibrillation in the dog heart in situ.** Journal of Pharmacology and Experimental Therapeutics. 216(1):39-44, 1981.

The effect of thioridazine on electrical and ischemic ventricular fibrillation in the dog heart in situ was assessed. In 30 chloralose anesthetized dogs, the repetitive response threshold was used to assess vulnerablity during right ventricular stimulation with transvenous catheter electrodes. Both 10mg/kg and 30/mg/kg of thioridazine increased diastolic excitability threshold while only the 30mg/kg dose widened QRS and prolonged Q-Tc. Repetitive response threshold was unchanged. In 45 pentobarbital anesthetized dogs, one stage ligation of the left anterior descending coronary artery was performed after pretreatment with placebo, 10mg/kg or 30mg/kg of thioridazine. Although thioridazine depressed excitability and had no effect on electrical fibrillation threshold, the 30mg/kg dose increased the likelihood of spontaneous ventricular fibrillation during acute ischemia. 41 references. (Author abstract modified)

002698 De Jong, Adrianus P.; Soudijn, Willem. Dept. of Pharmaceutical Chemistry, University of Amsterdam, Plantage Muidergracht 24, 1018 TV Amsterdam, The Netherlands **Relationships between structure and alpha-adrenergic receptor affinity of clonidine and some related cyclic amidines.** European Journal of Pharmacology. 69(2):175-188, 1981.

Of 43 cyclic amidines tested for ability to inhibit specific 3H-clonidine binding to alpha-adrenergic receptors in rat brain, oxymetazoline was the most potent. There was a good correlation between hypotensive activity and alpha2-adrenergic receptor affinity for some 2-(phenylimino)imidazolines. Apparent structural requirements for alpha2-receptor affinity included the presence of an aromatic moiety and au N-hydrogen in the heterocyclic ring. Ortho substitution in the phenyl ring was necessary for high affinity. 55 references. (Author abstract modified)

002699 DeFeudis, Francis V.; Ossola, Lucienne; Schmitt, Gaby; Wolff, Pierre; Mandel, Paul. Centre de Neurochimie, 11 rue Humann, F-67085 Strasbourg Cedex, France **Na-independent binding of (3H)GABA and (3H)muscimol to subcellular particles of neural primary cultures and whole brain.** Journal of Neurochemistry. 34(1):216-218, 1980.

The binding of 3H-GABA ((3H)gamma-aminobutyric acid) and 3H-muscimol to subcellular particles of Wistar rat whole brain and subcellular particles of neuron enriched and astroblast cultures were compared. Results showed that 3H-muscimol was bound to a greater extent than was 3H-GABA to particles of whole brain and of neuron enriched cultures. This finding suggests that muscimol receptors may exist not only in GABA synapses but also in other regions of neuronal membranes. Neither ligand was bound to astroblast particles, indicating the lack of receptor sites on glial membranes. 14 references.

002700 Demarest, K. T.; Moore, K. E. Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824 **Disruption of 5-hydroxytryptaminergic neuronal function blocks the action of morphine on tuberoinfundibular dopaminergic neurons.** Life Sciences. 28(12):1345-1351, 1981.

Subcutaneous injections of morphine to male rats were found to reduce dopamine (DA) turnover (alpha-methyltryrosine induced decline of DA concentrations) in the median eminence, and increased DA turnover in the striatum. Selective destruction of central 5-hydroxytryptamine (5-HT) neurons with intracerebroventricular injections of 5,7-dihydroxytryptamine, or the administration of metergoline, a putative 5-HT antagonist, blocked the inhibitory effects of morphine on DA turnover in the median eminence. In the same experiments, disruption of 5-HT neurotransmission processes caused similar but less dramatic antagonisms of the stimulatory actions of morphine on DA turnover in the striatum. Thus, 5-HT neurons play a role in mediating the effects of morphine on tuberoinfundibular and possibly on nigrostriatal DA neurons. 29 references. (Author abstract modified)

002701 Dettmar, Peter W.; Cowan, Alan; Walter, Donald S. Dept. of Pharmacology, Reckitt and Colman Pharmaceutical Div., Kingston-upon-Hull HU8 7DS, England **A comparison of the neurochemical effects of buprenorphine with those of morphine and haloperidol in rats.** European Journal of Pharmacology. 69(2):147-153, 1981.

The effects of buprenorphine (0.001 to 10mg/kg), haloperidol (0.01 to 3mg/kg), and morphine (1 to 30mg/kg) on the metabolism of noradrenaline (NA), dopamine (DA), and 5-hydroxytryptamine (5-HT) in male Sprague-Dawley rat brain were compared. Buprenorphine increased the rate of DA depletion after alpha-methyl-p-tyrosine (aMpT), but did not alter the rate of NA depletion. Similar results were obtained with haloperidol and morphine, except that the highest dose of morphine increased the aMpT induced depletion of NA. Naloxone antagonized the increased rate of DA depletion after aMpT in rats given buprenorphine, but not in rats given haloperidol. Naloxone also antagonized the increase in homovanillic acid caused by buprenorphine, but not that caused by haloperidol. It is suggested that buprenorphine, a partial agonist at mu-opiate receptors, may act on opiate receptors located presynaptically on dopaminergic neurons. 42 references. (Author abstract modified)

002702 Deutsch, J. A.; Parsons, S. L. Dept. of Psychology, University of California, San Diego, La Jolla, CA 92093 **Bombesin produces taste aversion in rats.** Behavioral and Neural Biology. 31(1):110-113, 1981.

The effects of bombesin (BBS) on the amount of food eaten were examined in eight male rats. A neutral flavor was paired with an injection of BBS, reported to reduce food intake, in a two bottle conditioned taste aversion test. The neutral flavor was significantly avoided. It is concluded that BBS reduces food intake through some aversive consequences and not through satiation. 8 references. (Author abstract modified)

002703 Dietl, H.; Sinha, J. N.; Philippu, A. Philippu: Dept. of Pharmacology and Toxicology of the University of Wurzburg, Versbacherstrasse 9, D-8700 Wurzburg, West Germany **Presynaptic regulation of the release of catecholamines in the cat hypothalamus.** Brain Research. 208(1):213-218, 1981.

To investigate the presynaptic regulation of the release of catecholamines in the cat hypothalamus, the posterior hypothalamus of cats was superfused through a push/pull cannula and the release of endogenous catecholamines was determined in the superfusate. Superfusion with yohimbine, isoprenaline, salbutamol, or tazolol increased, while superfusion with propranolol decreased, the release of all three catecholamines. Transection of the brain caudal to the hypothalamus inhibited resting and drug induced release. It is concluded that alpha-adrenoceptors and beta-adrenoceptors of the hypothalamus are involved in the regulation of the release of catecholamines. 20 references. (Author abstract modified)

002704 Dodd, Jane; Dingledine, Ray; Kelly, J. S. Kelly: Dept. of Pharmacology, St. George's Hospital Medical School, Jenner Wing, Cranmer Terrace, London SW17 ORE, England **The excitatory action of acetylcholine on hippocampal neurones of the guinea pig and rat maintained in vitro.** Brain Research. 207(1):109-127, 1981.

The excitatory action of acetylcholine (ACh) on hippocampal neurons of the guinea-pig and rat maintained in vitro was investigated. In preliminary experiments on 39 identified pyramidal cells in the in vitro slice preparation of the guinea-pig hippocampus, the depolarization evoked by ACh applied by microionotophoresis always was associated with an increase in membrane resistance. In nine slices cut from rat hippocampus, similar results were obtained from 24 cells. In a more detailed analysis on 13 cells from the rat hippocampus, whose mean resting potential was -74 mV and mean resting input resistance was 33 M Omega, the mean peak depolarization evoked by ACh was 11.6 mV and the mean increase in membrane resistance was 12 M Omega. It is suggested that the slow onset and offset of the responses evoked by ACh are not compatible with models based on diffusion and are best explained by postulating a sequential generation of one or more intermediates. 70 references. (Author abstract modified)

002705 Dupelj, M.; Geber, J. Dept. of Neurology, Medical Faculty, University of Zagreb, 41000 Zagreb, Yugoslavia **Dopamine as a possible neurotransmitter in the spinal cord.** Neuropharmacology. 20(2):145-148, 1981.

Pimozide, a dopamine receptor blocking agent, decreased the amplitude of the spinal monosynaptic mass reflex (MSMR) in spinalized cats, and this effect could not be reversed by L-DOPA. Disulfiram, which inhibits synthesis of noradrenaline from dopamine, induced a moderate increase in MSMR amplitude, and L-DOPA reinforced the effect of disulfiram. Results provided indirect evidence of dopaminergic neurotransmission in the spinal cord. 17 references. (Author abstract modified)

002706 Dyck, Lillian E. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, Canada S7N 0X0 **Methylphenidate-like stimulants in vitro release (3H)tyramines but not (14C)dopamine.** European Journal of Pharmacology. 69(3):371-374, 1981.

The effects of methylphenidate, cocaine, nomifensine, and amfonelic acid on the uptake and release of dopamine, m-tyramine, and p-tyramine in male Wistar rat striatal slices were examined. All four stimulants inhibited the uptake of (14C)dopamine, (3H)p-tyramine, and (3H)m-tyramine; the drugs stimulated release of (3H)p-tyramine and (3H)m-tyramine, but not (14C)dopamine. The methylphenidate like stimulants also antagonized the release of (14C)dopamine and (3H)p-tyramine induced by d-amphetamine. Results suggest that the tyramines are transported independently from dopamine. 10 references. (Author abstract modified)

002707 Dyer, R. G.; Murugaiah, K.; Theodorou, A.; Clow, A.; Jenner, P.; Marsden, C. D. Agricultural Research Council, Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **During one year's neuroleptic treatment in rats striatal dopamine receptor blockade decreases but serum prolactin levels remain elevated.** Life Sciences. 28(2):167-174, 1981.

The effects of chronic treatment (for 1 year) with either trifluoperazine dihydrochloride or thioridazine dihydrochloride on serum prolactin levels and striatal dopamine receptor function were investigated. Serum prolactin levels at the end of the year remained elevated compared to those in control animals, and the elevation was no different from that obtained by administration of an equivalent acute single oral bolus. In contrast, the inhibition of apomorphine induced stereotypy produced by the acute administration of either drug disappeared during chronic treatment, to be replaced after a year's neuroleptic administration by a supersensitive response. Similarly, the increase in dopamine turnover produced by acute neuroleptic administration, evidenced by raised striatal 3,4-dihydroxyphenylacetic acid levels, also disappeared at the end of a year's treatment, when specific binding of 3H-spiperone to striatal homogenates indicated an increased number of dopamine receptors. 28 references. (Author abstract modified)

002708 Dyer, Robert S.; Howell, William E.; MacPhail, Robert C. Neurotoxicology Division, Health Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711 **Dopamine depletion slows retinal transmission.** Experimental Neurology. 71(2):326-340, 1981.

In male hooded rats, depletion of norepinephrine and dopamine by alpha-methyl-paratyrosine (AMT) was found to increase significantly the latencies of early peaks in flash evoked potentials recorded from the visual cortex, lateral geniculate nucleus, and optic tract. These effects were not produced by depletion of norepinephrine by FLA-63, blockade of muscarinic acetylcholine receptors by scopolamine, or blockade of opiate receptors by naloxone. AMT effects occurred only when flashes were used; optic tract stimulation failed to reveal the drug induced changes. In a dose/response study, haloperidol produced effects similar to those of AMT. L-dopa plus R04-4602 reversed some of the effects of AMT. It is concluded that depletion of retinal dopamine impairs the timing of retinal responses to light. 19 references. (Author abstract)

002709 Eikelboom, Roelof; Stewart, Jane. Stewart: Dept. of Psychology, Concordia University, 1455 de Maisonneuve Blvd. West, Montreal, Quebec, Canada H3G 1M8 **Temporal and environmental cues in conditioned hypothermia and hyperthermia associated with morphine.** Psychopharmacology. 72(2):147-153, 1981.

The effectiveness of temporal and environmental cues in eliciting conditioned hypothermia and hyperthermia was studied in male Wistar rats using an i.p. injection of morphine sulphate as the unconditioned stimulus. The relevance of temporal stimuli was minimized in Experiment 1 by administering morphine at irregular times on alternate days. For one group, morphine injections were preceded and followed by periods in distinctive environments. A second group, though exposed to the environments, received morphine in the home cage on the intervening days. All animals receiving morphine showed a nonspecific hypothermia when not under the direct influence of morphine. A conditioned hyperthermia was evident in the first group in the distinctive environments. In Experiment 2, in which animals remained in their home cages at all times, the relevance of temporal cues was emphasized by administering morphine at exactly 24 hour intervals. These animals became hypothermic only around the time of the expected injection. Animals in another group that received morphine at irregular times showed the nonspecific hypothermia seen previously. There was no evidence for a conditioned hyperthermia in Experiment 2. 28 references. (Author abstract modified)

002710 Eikelboom, Roelof; Stewart, Jane. Dept. of Psychology, Concordia University, 1455 de Maisonneuve Blvd., Montreal, Canada H3G 1M8 **Hypophysectomy increases the sensitivity of rats to naloxone-induced hypothermia.** Life Sciences. 28(9):1047-1052, 1981.

The role of pituitary endorphins in thermoregulation was explored in three experiments. Hypophysectomized rats were found to be hypothermic when compared to intact rats, but showed a hyperthermic response to handling induced stress of equal magnitude to that seen in intact animals. In unstressed, intact, and hypophysectomized animals, the specific opiate antagonist, naloxone, produced a dose dependent hypothermia, but hypophysectomized animals were found to be 10 times more sensitive to naloxone than were the intact animals. In contrast, short-term blockade of pituitary endorphins by dexamethasone had no effect on the magnitude of the naloxone induced hypothermia. It is concluded that endorphins of pituitary origin play a long-term tonic role in the modulation of the sensitivity of the brain opioid systems. 21 references. (Author abstract modified)

002711 Ellinwood, E. H., Jr.; Kilbey, M. Marlyne. Behavioral Neuropharmacology Section, Dept. of Psychiatry, Duke University Medical Center, Durham, NC 27710 **Fundamental mechanisms underlying altered behavior following chronic administration of psychomotor stimulants.** Biological Psychiatry. 15(5):749-757, 1980.

Fundamental mechanisms underlying altered behavior following chronic administration of psychomotor stimulants are described, and the utility of the chronic psychomotor stimulant model of human psychotic behavior is evaluated. The altered behavior which occurs with chronic administration of psychomotor stimulants appears to be attributable to five major phenomena. One of these, conditioning, involves a global reorganization whose biological bases are little understood. Alterations reflecting kindling mechanisms represent changes in membrane mechanisms resulting in enhanced propagation of electrical signals. A third mechanism involves adaptation of drug metabolism systems, and the final two involve aminergic neuronal functon, i.e., decreased levels of dopamine and possibly alterations in other amine systems and increased number of dopamine receptors. Evidence linking behavioral reorganization as a result of chronic administration of psychomotor stimulants with these phenomena is presented. 58 references. (Author abstract modified)

002712 End, David W.; Carchman, Richard A.; Dewey, William L. Dewey: Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Interactions of narcotics with synaptosomal calcium transport.** Biochemical Pharmacology. 30(6):674-676, 1981.

The effects of morphine on a process of nerve terminal Ca2 transport which is relevant to excitation/secretion coupling were investigated using the in vitro model developed by Blaustein et al. (1970). Morphine selectively blocked the synaptosomal 45Ca2 uptake induced by depolorization with 60mM KCl. Since the potassium induced influx of Ca2 previously has been shown to be obligatory to synaptosomal secretion coupling, the present findings may represent a molecular mechanism contributing to the antisecretory activity of the narcotics. The relevance of these in vitro neurochemical alterations to specific aspects of the pharmacological activity of morphine is discussed. 35 references.

002713 Enna, S. J.; Ferkany, J. W.; Butler, I. J. Dept. of Pharmacology, University of Texas Medical School at Houston, Houston, TX 77025 **Chronology of neurochemical alterations induced by GABA agonist administration.** Advances in Biochemical Psychopharmacology. 26:181-189, 1981.

The time course and reversibility of receptor alterations (increase in dopamine receptor binding and function and decrease in GABA receptor binding in the rat corpus striatum) induced by chronic administration of either GABA-transaminase (GABA-T) inhibitors or direct acting agonists were investigated. Results indicate that the GABA receptor binding changes precede the dopamine receptor alterations and that both receptor binding changes precede the dopamine receptor alterations and that both receptor changes are completely reversible following cessation of treatment. In addition, the data reveal that the time course of the receptor changes observed does not correlate with the elevation in brain GABA content induced by the GABA-T inhibitor. Furthermore, other findings suggest that tolerance may develop to some of the neurochemical changes induced by acute treatment with GABA agonists. 21 references.

002714 Faden, Alan I.; Jacobs, Thomas P.; Holaday, John W. Dept. of Medical Neurosciences, Walter Reed Army Institute of Research, Washington, DC 20012 **Opiate antagonist improves neurologic recovery after spinal injury.** Science 211(4481):493-494, 1981.

The opiate antagonist naloxone has been used to treat cats subjected to cervical spinal trauma. In contrast to saline treated controls, naloxone treatment significantly improved neurological recovery. Because naloxone significantly elevates mean arterial pressure in the cat, it is suggested that the beneficial effects of naloxone result from its ability to secondarily improve local spinal cord blood flow. These findings implicate endorphins in the pathophysiology of spinal cord injury, and indicate that narcotic antagonists may have a therapeutic role in this condition. 28 references. (Author abstract modified)

002715 Feldberg, W.; Rocha E Silva, M., Jr. National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Inhibition of vasopressin release to carotid occlusion by gamma-aminobutyric acid and glycine.** British Journal of Pharmacology. 72(1):17-24, 1981.

When applied to the ventral surface of the brainstem between medulla and cord, GABA and glycine markedly attenuated the vasopressin release in response to carotid occlusion in anesthetized cats. Glycine was effective in a concentration of 0.1mg/ml and was about 100 times more potent than GABA. The pressor response to carotid occlusion was not altered. When the amino acids were applied to a more rostral region, they attenuated the pressor response to carotid occlusion, but did not alter vasopressin release. 23 references. (Author abstract modified)

002716 Ferkany, J. W.; Strong, R.; Enna, S. J. Enna: Dept. of Pharmacology, University of Texas Medical School, Houston, TX 77025 **Dopamine receptor supersensitivity in the corpus striatum following chronic elevation of brain gamma-aminobutyric acid.** Journal of Neurochemistry. 34(1):247-249, 1980.

Brain dopamine and gamma-aminobutyric acid (GABA) receptor binding were studied in male Sprague-Dawley rats treated for 15 days with aminooxyacetic acid, isonicotinic acid hydrazide, or gamma-acetylenic GABA. Chronic treatment with the GABA transaminase inhibitors elevated brain GABA content and produced a significant increase in the number of dopamine receptors and caused a significant decrease in GABA receptors in the corpus striatum. Female mice treated with the GABA transaminase inhibitors showed increased apomorphine gnawing responses, this is suggestive of the functional supersensitivity of the striatal dopamine receptors. 19 references.

002717 Feuerstein, G.; Zilberman, Y.; Hemmendinger, R.; Lichtenberg, D. NIMH, Lab. of Clinical Sciences, Building 10, Room 2D-53, 9000 Rockville Pike, Bethesda, MD 20205 **Attenuation of the lithium-induced diabetes-insipidus-like syndrome by amiloride in rats.** Neuropsychobiology. 7(2):67-73, 1981.

The effect of amiloride on lithium induced polydipsia and polyuria and on the lithium concentration in the plasma, brain, kidney, thyroid, and red blood cells was investigated in rats chronically treated with LiCl. Amiloride reduced the drinking and urine volume of rats in an acute (6 or 12 h) and a subacute (3 days) experiment. Six hours after the administration of amiloride, a reduction was observed in the lithium content of the renal medulla but not in the other organs studied. At 12 h, all the tissues showed a slight increase in lithium levels. After 3 days of combined treatment, a marked elevation in plasma and tissue lithium levels accompanied a reduction in water intake. In all the experiments, the attenuation of the litium induced diabetes insipidus like syndrome by amiloride was accompanied by a reduction of the ratio between the lithium concentration in the renal medulla and its levels in the blood and an elevation in the plasma potassium level. It is concluded that acute amiloride administration to lithium treated patients suffering from polydipsia and polyuria might relieve these patients but prolonged amiloride supplementation would result in elevated lithium levels and might be hazardous. 13 references. (Author abstract)

002718 Finnerty, E. P.; Chan, S. H. H. Dept. of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN 55455 **The participation of substantia nigra zona compacta and zona reticulata neurons in morphine suppression of caudate spontaneous neuronal activities in the rat.** Neuropharmacology. 20(3):241-246, 1981.

Morphine (5mg/kg i.v.) depressed single unit activity in the caudate nucleus and substantia nigra zona reticulata of lightly anesthetized rats and increased activity in the substantia nigra zona compacta. These effects were reversed by naloxone (1mg/kg i.v.). Microinjection of morphine into the zona compacta induced a naloxone reversible depression of caudate activity. Direct nigral application of strychnine induced a moderate decrease in caudate activity and an increase in zona compacta discharges. Morphine (5mg/kg i.v.) enhanced the effects of strychnine and depressed reticulata neurons. Results suggest that morphine suppresses caudate spontaneous activity by activating nigrostriatal neurons and inactivating a novel striatonigral pathway. The latter may incorporate reticulata neurons, which may exert tonic inhibition on the compacta cells, possibly using glycine as a neurotransmitter. 34 references. (Author abstract modified)

002719 Forchetti, Concetta M.; Meek, James L. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Evidence for a tonic GABAergic control of serotonin neurons in the median raphe nucleus.** Brain Research. 206(1):208-212, 1981.

Evidence for a tonic GABAergic control of serotonin neurons in the median raphe nucleus is described. Injection into the median raphe nucleus of the GABA antagonists picrotoxin and bicuculline and the GABA agonist muscimol increase and decrease, respectively, the serotonin (5-HT) turnover and the steady-state content of 5-hydroxyindoleacetic acid. Results indicate that the inhibitory effect of GABA on 5-HT neuronal activity in the median raphe nucleus is potentiated by benzodiazepines. Although the hypothesis that the clinically important antianxiety effects of diazepam may be due to its modulation of the GABA 5-HT system requires much more research, these data provide evidence that the proposed interaction of benzodiazepines, GABA, and 5-HT can occur. 16 references. (Author abstract modified)

002720 Frederickson, Robert C. A.; Smithwick, Edward L.; Shuman, Robert; Bemis, Kerry G. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46285 **Metkephamid, a systemically active analog of methionine enkephalin with potent opioid delta-receptor activity.** Science. 211(4482):603-605, 1981.

The synthesis and pharmacological testing of a minimally modified analog of methionine enkephalin, that is a systemically active analgesic that has high affinity for the delta receptor, is reported. Since it is at least 100 times potent more than morphine as an analgesic when placed directly into the lateral ventricles and is 30 to 100 times more potent on the delta receptor and yet is roughly equipotent on the mc receptor in vitro, it is concluded that it probably produces analgesia by an action on delta receptors as well as, or rather than, on mc receptors. Experiments with metkephamid in rats are described and it is noted that the drug had less of a tendency to produce respiratory depression, tolerance, and physical dependence than standard analgesics. 23 references. (Author abstract modified)

002721 Freedman, Mark S.; Clark, Bruce D.; Cruz, Tony F.; Gurd, James W.; Brown, Ian R. Brown: Dept. of Zoology, Scarborough College, University of Toronto, West Hill, Ontario M1C 1A4, Canada **Selective effects of LSD and hyperthermia on the synthesis of synaptic proteins and glycoproteins.** Brain Research. 207(1):129-145, 1981.

The selective effects of LSD and hyperthermia on the synthesis of synaptic proteins and glycoproteins were investigated. Protein synthesis in rabbit brain was inhibited following the intravenous injection of LSD. The incorporation of (35S)methionine into brain microsomal and synaptic fractions was decreased by 35% to 45% relative to control values. A selective increase was observed, however, in the relative labeling of a protein of molecular weight 75,000 daltons. When LSD induced hyperthermia was blocked, the general reduction in labeling of microsomal and synaptic proteins still was apparent but the selective increase in relative labeling of the 75,000 dalton protein was not evident. Induction of hyperthermia by means other than LSD produced selective increases in the relative labeling of microsomal and synaptic proteins of molecular weight 75,000 and 95,000 daltons. LSD did not alter the synthesis of synaptic glycoproteins, but it did reduce the synthesis of glycosylated proteins present in the other subcelluler fractions. Results suggest that LSD induces selective changes in the synthesis of brain proteins and that the synthesis of synaptic glycoproteins may relatively be resistant to drug administration. 45 references. (Author abstract modified)

002722 Freedman, S. B.; Poat, Judith A.; Woodruff, G. N. Woodruff: Dept. of Physiology and Pharmacology, University of Southamptom, Bassett Crescent East, Southampton S09 3TU, England **The effect of guanosine nucleotides on (3H)sulpiride binding to rat striatal membranes.** European Journal of Pharmacology. 69(1):117-118, 1981.

Drug competition for 3H-sulpiride binding sites in rat striatal membranes was studied in the presence and absence of guanosine nucleotides. Results showed that the guanosine nucleotides decreased the affinity of dopamine agonists for 3H-sulpiride binding sites. These results are not consistent with the current classification of dopamine receptors as D1 (adenylate cyclase linked) and D2 (nonlinked) receptors. 5 references.

002723 Friedman, David P.; Horvath, Fred E. Laboratory of Neuropsychology, NIMH, Bldg. 9, NIH, Bethesda, MD 20205 **Catecholaminergic involvement in phasic versus tonic electrocortical arousal.** Brain Research. 194(2):572-577, 1980.

Short duration, phasically induced arousal was pharmacologically differentiated from long duration, tonic arousal in encephale isole cats. Pretreatment with reserpine (0.4mg/kg) to deplete catecholamines resulted in a selective reduction in the intensity and duration of arousal induced by phasic activation of the reticular formation. Background levels of tonic arousal were not altered by reserpinization. The effects of reserpine on electrocorticogram measures of arousal were not altered by manipulation of 5-hydroxytryptamine levels. 20 references.

002724 Fromm, Gerhard H.; Glass, Jay D.; Chattha, Amrik S.; Martinez, A. Julio. Dept. of Neurology, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261 **Effect of anticonvulsant drugs on inhibitory and excitatory pathways.** Epilepsia. 22(1):65-73, 1981.

The effect of anticonvulsant drugs on inhibitory and excitatory pathways was investigated in cats. A conditioning stimulus to the periventricular gray matter inhibits the response of spinal trigeminal neurons to maxillary nerve stimulation. Sodium valproate and ethosuximide decrease the periventricular inhibition without significantly affecting the response of these neurons to the unconditioned maxillary nerve stimulus. It is reported that carbamazepine and phenytoin decrease the response to the unconditioned maxillary nerve stimulus, and only depress the periventricular inhibition secondarily. These results further support the hypothesis that the ability to depress selectively inhibitory pathways in the CNS is an important characteristic of antiabsence drugs, and that absence seizures may represent paroxysmal discharges in inhibitory pathways. 38 references. (Author abstract modified)

002725 Fujimoto, Masafumi; Okabayashi, Tadashi. Shionogi Research Laboratories. Shionogi and Co., Ltd., Fukushima-ku, Osaka 553, Japan **Effect of picrotoxin on benzodiazepine receptors and GABA receptors with reference to the effect of Cl- ion.** Life Sciences. 28(8):895-901, 1981.

In the presence of Cl- ion plus low concentrations of GABA, picrotoxin was found to modulate specific (3H)diazepam and (3H)muscimol binding in membranes from rat cerebellum. In the presence of higher concentrations of GABA, picrotoxin inhibited (3H)diazepam binding. This inhibition seems to be the result of reduced GABA binding, which occurred in the presence of picrotoxin and Cl- ion. These results may indicate that benzodiazepine receptors, GABA receptors, and the Cl- ionophore are closely associated with each other. 17 references. (Author abstract modified)

002726 Fuller, R. W.; Snoddy, H. D. Lilly Research Laboratory, Eli Lilly and Co., Indianapolis, IN **Effect of mazindol on brain dopamine turnover in spiperone-treated rats.** Journal of Neural Transmission. 44:13-19, 1979.

Evidence is presented that mazindol, an anorexic drug, causes a large increase in brain 3,4-dihydroxyphenylacetic acid (DOPAC) concentration in spiperone pretreated rats. The increase was dose related over a 1mg/kg to 10mg/kg dose range of mazindol and reached maximum within 1 hour after mazindol injection into rats pretreated 1 hour previously with spiperone. In spiperone pretreated rats, mazindol accelerated the disappearance of dopamine after inhibition of dopamine synthesis by alpha-methyltyrosine. Mazindol apparently resembles amfonelic acid, methylphenidate, and cocaine in facilitating the impulse mediated release of dopamine. (Journal abstract)

002727 Fuxe, K.; Kohler, C.; Agnati, L. F.; Andersson, K.; Ogren, S. -O.; Eneroth, P.; Perez-de-la-Mora, M.; Karobath, M.; Krogsgaard-Larsen, P. Dept. of Histology, Karolinska Institutet, S-104 01 Stockholm, Sweden **GABA and benzodiazepine receptors. Studies on their localization in the hippocampus and their interaction with central dopamine neurons in the rat brain.** Advances in Biochemical Psychopharmacology. 26:61-76, 1981.

The binding of 3H-GABA, 3H-muscimol, and 3H-flunitrazepam in the hippocampus of the rat after lesions of intrinsic cell bodies and transections of various cholinergic and glutamatergic afferents to the hippocampus were investigated. GABA-monoamine interactions were examined in studies of the effects of the GABA transaminase inhibitor, gabuculine, the GABA agonist THIP, and a new GABA mimetic drug, GA 30-905, on monoamine turnover. The effects of SQ 20009, alone and in combination with flunitrazepam or gabaculine, on monoamine turnover were analyzed. By measuring the dopamine turnover in the lateral septal region following ibotenic acid lesions of hippocampal pyramidal cells which are known to give rise to the glutamate innervation of the lateral septum, evidence is provided that glutamatergic pathways may control turnover of the central dopamine pathways. 29 references.

002728 Garcia-Sainz, J. Adolfo; Li, Shih-Ying; Fain, John N. Section of Physiological Chemistry, Division of Biology and Medicine, Brown University, Providence, RI 02912 **Alpha2 adrenergic amines, adenosine and prostaglandins inhibit lipolysis and cyclic AMP accumulation in hamster adipocytes in the absence of extracellular sodium.** Life Sciences. 28(4):401-406, 1981.

The accumulation of cyclic AMP due to adenosine deaminase plus theophylline and either isoproterenol or adrenocorticotropic hormone in the presence of adenosine deaminase plus theophylline, was inhibited by clonidine, N6-(phenylisopropyl)-adenosine and prostaglandin E2. The inhibition was nearly identical in medium containing sodium ions or in medium in which sodium and its accompanying anion were substituted by an isosmotic amount of sucrose. Consistent with this, lipolysis induced by adenosine deaminase and theophylline was significantly inhibited by clonidine, N6-(phenylisopropyl)-adenosine and prostaglandin E2 regardless of the presence or absence of NA in the medium. Results do not support the suggestion that extracellular Na is required for the regulation of cyclic AMP levels by hormones and neurotransmitters that inhibit adenylate cyclase. 17 references. (Author abstract modified)

002729 Garthwaite, John; Regan, Ciaran M. MRC Developmental Neurobiology Unit, Institute of Neurology, 33, John's Mews, London WC1 2NS, England **Toxic effects of alpha-aminoadipate on cultured cerebellar cells.** Brain Research. 194(2):603-607, 1980.

The cytotoxic effects of alpha-aminoadipate (aAA) on cultures of rat cerebellar neurons and nonneuronal cells were studied, and the goals were: to determine whether the selective toxic actions of aAA could be reproduced in vitro, to evaluate aAA's potential utilization in deleting nonneuronal cells from primary neural cultures, and to determine whether aAA's toxiciting is attributable to only one of the isomers. Although the excitatory amino acid antagonist properties of aAA are specific to the D-isomer, toxic properties were associated solely with the L-isomer. L-aAA produced death in cultured neurons, but only at concentrations that were toxic also to nonneuronal cells. 22 references.

002730 Gavish, Moshe; Snyder, Solomon H. Snyder: Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Benzodiazepine recognition sites on GABA receptors.** Nature. 287(5783):651-652, 1980.

GABA receptors labelled by 3H-muscimol were shown to possess a benzodiazepine recognition site. Benzodiazepines, in proportion to their pharmacological activity, protect 3H-muscimol binding from inactivation by heat and the protein modifying reagent iodoacetamide. GABAergic agents and benzodiazepines were found to exert their protective effects at distinct recognition sites both on the receptors labelled by 3H-flunitrazepam and on those labelled by 3H-muscimol. The synergistic interactions of GABA and diazepam in protecting these receptors suggest that the two sites are allosterically linked. 16 references. (Author abstract modified)

002731 Gekiere, Francoise; Allegre, Guy; Brindeau, Francoise; Borenstein, Pinchas. Ecole Pratique des Hautes Etudes, 54, Avenue de la Republique, F-94800 Villejuif, France **/The action of benzodiazepines on the limbic system compared to other tranquilizers./** Action des benzodiazepines sur le systeme limbique par rapport a d'autres tranquillisants. Psychologie Medicale. 12(11):2369-2372, 1980.

The effects of benzodiazepines on an animal's limbic system as compared to tranquilizers are studied. A group of cats was administered one of eight benzodiazepines, and, after a certain time interval, a tranquilizer was administered to each cat. The differences in EEG recordings were reported. Results indicate that the benzooiazepines demonstrate a hippocampic delta effect not seen in the tranquilizers. The sedative effects of the drugs remain ambiguous. 2 references. (Journal abstract modified)

002732 Geller, Herbert M. Dept. of Pharmacology, C.M.D.N.J.-Rutgers Medical School, Piscataway, NJ 08854 **Histamine actions on activity of cultured hypothalamic neurons: evidence for mediation by H1- and H2-histamine receptors.** Developmental Brain Research. 1(1):89-101, 1981.

Tuberal hypothalamic tissue cultures were used to investigate the actions of histaminergic agents on neuronal activity using extracellular glass micropipettes. Histamine and H1 and H2 agonists were applied locally onto single active neurons by iontophoresis, while histaminergic antagonists were perfused through the bathing medium. Perievent histogram and ratemeter analysis showed histamine to both excite and depress unit activity. Excitations were only antagonized by putative H1 and not H2 histamine antagonists, whereas inhibitions were antagonized by H2 and not H1 antagonists. Dimaprit, a specific H2 agonist, elicited inhibitions of activity, while 2-(2-pyridyl)ethylamine, a putative H1 agonist, elicited both excitations and inhibitions. Two pharmacologically distinct populations of histamine receptors may exit in the hypothalamus: excitatory H1 receptors and inhibitiory H2 receptors. 41 references. (Author abstract)

002733 Giorguieff-Chesselet, M. F.; Kemel, M. L.; Glowinski, J. no address **The presynaptic stimulating effect of acetylcholine on dopamine release is suppressed during activation of nigro-striatal dopaminergic neurons in the cat.** Neuroscience Letters. 14:177-182, 1979.

Evidence is presented that acetylcholine (ACh) in the presence of eserine stimulates the release of (3H)dopamine (DA) continuously formed from (3H)tyrosine when delivered to a push/pull cannula implanted in the left caudate nucleus of halothane anesthetized cats. This effect is transient and is followed by a second increase in (3H)DA release after removal of ACh and eserine. These changes in (3H)DA release during and after ACh application were no longer seen during activation of the dopaminergic neurons by continuous delivery of substance-P to the ipsilateral substantia nigra (SN). These results indicate that the presynaptic regulations of DA release by ACh is dependent on the rate of firing of nigrostriatal dopaminergic neurons. (Journal abstract)

002734 Goldberg, Michael R.; Gerkens, John F.; Oates, John A.; Robertson, David. Div. of Clinical Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232 **Alpha-methylepinephrine, a methyldopa metabolite that binds to alpha-receptors in rat brain.** European Journal of Pharmacology. 69(1):95-99, 1981.

The abilities of epinephrine (EPI), norepinephrine (NE), methyldopa (MD), methylnorepinephrine (MeNE), and methylepinephrine (MeEPI) to compete for 3H-WB-4101 binding sites (alpha1-receptors) and 3H-clonidine binding sites (alpha2-receptors) in male Sprague-Dawley rat brain were compared. The descending order of potency in competing for 3H-WB-4101 binding sites was: EPI and NE, MeNE, MeEPI, MD. For the 3H-clonidine binding site, the descending order of potency was: EPI, MeNE, NE, MeEPI, MD. It is suggested that MeEPI may be the centrally active metabolite through which MD exerts its antihypertensive effect. 11 references. (Author abstract modified)

002735 Gomes, Urbolino C. R.; McCarthy, Brian W.; Shanley, Brian C. Shanley: Dept. of Biochemistry, University of Queensland, St. Lucia, Brisbane, 4067 Australia **Effect of neuroleptics on indoleamine-N-methyltransferase activity and brain metabolism of bufotenin.** Biochemical Pharmacology. 30(6):571-575, 1981.

A range of neuroleptics, nonneuroleptic phenothiazines, and antidepressants were tested for their ability to inhibit purified rabbit lung indoleamine-N-methyltransferase (INMT) and to modify the metabolism of (3H)bufotenin administered intraventricularly. Benperidol and droperiodol proved to be the most potent inhibitors of INMT among the compounds tested. On the other hand, trifluperidol and haloperidol showed no inhibitory activity at concentrations up to 2.5mM, while chlorpromazine, thioridazine, pericyazine and perphenazine were effective only at 250mcM or 2.5mM. Oxidative deamination was shown to be an important pathway in normal rat brain for the metabolism of bufotenin. Of the drugs tested only chlorpromazine elevated the brain ratio of (3H)bufotenin to (3H)5-hydroxyindoleacetic acid whereas primozide and thiothixene caused a decrease in this ratio. These findings suggest that neuroleptic drugs in general do not exert their antipsychotic effects by inhibiting the synthesis or accelerating the oxidative deamination of N,N-dimethylated indoleamines. 29 references. (Author abstract modified)

002736 Gonzalez, J. P.; Sewell, R. D. E.; Spencer, P. S. J. Division of Pharmacology, Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cardiff, Wales CF1 3NU **Dopaminergic involvement in the hyperalgesic effect of nomifensine.** Life Sciences. 28(8):951-956, 1981.

Nomifensine, a potent inhibitor of both noradrenaline and dopamine reuptake, was found to produce a dose related hyperalgesia in the tail immersion test, using a 45 degrees C stimulus. This activity was abolished by the dopamine antagonists haloperidol and pimozide, but remained unchanged by the relatively selective adrenergic antagonists phentolamine, phenoxybenzamine or propranolol. Thus, it is postulated that there is a dopaminergic involvement in nomifensine hyperalgesia to the exclusion of an adrenergic mechanism. The paradoxical involvement of dopamine in opiate analgesia is discussed in relation to hyperalesia mediated through dopaminergic pathways. 35 references. (Author abstract)

002737 Gordon, C. J.; Heath, J. E. Experimental Biology Division, Environmental Protection Agency, Research Triangle Park, NC 27711 **Temporal patterning of neuronal activity during thermal and neurochemical stimulation of the preoptic/anterior hypothalamus of the awake rabbit.** Neuropharmacology. 20(2):163-168, 1981.

Recordings of preoptic/anterior hypothalamic (POAH) unit activity during POAH cooling were examined for changes in the distribution of interspike intervals (ISI) and coefficient of variation (CV). Cold sensitive neurons showed greater shifts in CV during cooling than warm sensitive or thermoneutral units. Norepinephrine, 5-hydroxytryptamine, and prostaglandin-E2 promoted specific changes in the CV that varied with thermal state. Interconversions between normal, gamma, truncated Poisson, and bimodal ISI distributions were occasionally observed. Results indicate that neurotropic agents can alter the temporal and spatial mechanisms of neuronal integration in the POAH. 20 references. (Author abstract modified)

002738 Grandison, Lindsey. Dept. of Physiology, College of Medicine and Dentistry of New Jersey, Piscataway, NJ 08854 **Anterior pituitary GABA receptors and their regulation of prolac-**

tin secretion. Advances in Biochemical Psychopharmacology. 26:219-227, 1981.

The regulation of prolactin secretion by anterior pituitary GABA receptors was investigated via examination of the effects of the potent and long-acting GABA agonist muscimol on prolactin release. Results indicate that both GABA and GABA agonists can inhibit proclactin release. This response results from the action of GABA agonists on the anterior pituitary gland. This action is both specific and receptor mediated. Blockade of the receptor with a specific receptor antagonist prevents the action on prolactin release. Moreover, specific GABA binding sites have been detected on rat and human anterior pituitary tissue. This GABA inhibitory system is separate from the well established dopamine inhibition of prolactin release. 24 references.

002739 Green, Vicki. Dept. of Psychology, Oklahoma State University, Stillwater, OK 74078 **Adrenal hormones and ethanol ingestion in C57BL/Crgl and C3H/Crgl/2 mice.** Behavioral and Neural Biology. 31(1):56-66, 1981.

The effects of two kinds of corticoid injections (a glucocorticoid and a mineralocorticoid) on the alcohol consumption of two inbred strains of mice were examined. The alcohol consumption of C57BL/Crgl mice decreased significantly when animals of this strain were injected with a solution of 0.2mg of hydrocortisone acetate (a glucocorticoid) every second day. No such significant decrease in alcohol consumption occurred when C3H/Crgl/2 mice were injected with the same solution daily. When administered a solution of 0.5mg of deoxycorticosterone acetate (a mineralocorticoid), neither the C57BL/Crgl injected daily or every other day nor the C3H/Crgl/2 injected daily displayed a significant decrease in alcohol consumption. The results indicate possible involvement of glucocorticoids, rather than mineralocorticoids, in the alcohol preference of mice. 18 references. (Author abstract modified)

002740 Griersmith, B. T.; Duggan, A. W.; North, R. A. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, Australia **Methysergide and supraspinal inhibition of the spinal transmission of nociceptive information in the anaesthetized cat.** Brain Research. 204(1):147-158, 1981.

In anesthetized cats methysergide was administered while measuring tonically present supraspinal inhibition of excitation of lumbar dorsal horn neurones by cutaneous noxious stimuli or by impulses in unmyelinated primary afferents. In some experiments, inhibition was produced by electrical stimulation near the medullary raphe. Methysergide did not reduce supraspinal inhibition when administered electrophoretically either near the bodies of dorsal horn neurons, in the region of the substantia gelatinosa, or topically to the dorsal surface of the spinal cord. Administered intravenously in doses of up to 2.0mg/kg, methysergide depressed the spinal transmission of nociceptive information and reduced supraspinal inhibition. This latter effect does not result from a blockade of the action of serotonin released by descending fibers, but rather from a depression of the firing of the cells of origin. 43 references. (Author abstract modified)

002741 Griffin, H. D.; Sykes, M.; Hawthorne, J. N. Hawthorne: Dept. of Biochemistry, University of Nottingham Medical School, Queen's Medical Center, Nottingham NG7 2UH, England **Effects of neomycin on calcium and polyphosphoinositide metabolism of guinea pig synaptosomes.** Journal of Neurochemistry. 34(3):750-752, 1980.

The effects of neomycin on polyphosphoinositide metabolism in intact synaptosomes from guinea-pig brain were studied. Results indicated that neomycin did not readily enter intact synaptosomes and that its binding to the external surface of the synaptosomal plasma membrane restricted calcium entry through calcium and sodium ion channels. It is suggested that neomycin may alter polyphosphoinositide metabolism indirectly, by acting on calcium metabolism, rather than by interacting directly with phospholipids. 10 references.

002742 Gross, Gerhard; Schumann, Hans-Joachim. Schumann: Institut fur Pharmakologie, Universitat Essen, Hufelandstrasse 55, D-4300 Essen, West Germany **Enhancement of noradrenaline release from rat cerebral cortex by neuroleptic drugs.** Naunyn-Schmiedeberg's Archives of Pharmacology. 315(2):103-109, 1980.

Levomepromazine, haloperidol, thioridazine, clozapine, and sulpiride all increased the tritium efflux from electrically stimulated slices of male Sprague-Dawley rat parieto-occipital cortex preincubated in 3H-noradrenaline. The neuroleptics enhanced the stimulation induced noradrenaline release primarily by acting on presynaptic alpha-adrenoceptors. Clozapine, the most potent neuroleptic tested, also inhibited uptake of noradrenaline. Amitriptyline, a tricyclic antidepressant, increased transmitter efflux at the same concentrations and to a similar extent as the neuroleptics. 33 references. (Author abstract modified)

002743 Guarneri, P.; Corda, M. G.; Concas, A.; Biggio, G. Biggio: Institute of Pharmacology, School of Biology, University of Cagliari, Cagliari, Italy **Kainic acid-induced lesion of rat retina: differential effect on cyclic GMP and benzodiazepine and GABA receptors.** Brain Research. 209(1):216-220, 1981.

Intraocular injection of kainic acid was found to cause a marked decrease in GABA content in the rat retina and almost complete loss of glutamate decarboxylase activity in this tissue, within 3 days. Morevover, kainic acid produced a decrease of approximately 65% in the number of both (3H)diazepam and (3H)GABA binding sites without changing the apparent dissociation constants for their ligands. In contrast to that in brain areas, cyclic GMP content in the retina is neither influenced by kainic acid nor by the systemic administration of diazepam and muscimol. 20 references. (Author abstract)

002744 Guerri, Consuelo; Ribelles, Milagro; Grisolia, Santiago. Instituto de Investigaciones Citologicas de la Caja de Ahorros de Valencia, Amadeo de Saboya, 4, Valencia 10, Spain **Effects of lithium, and lithium and alcohol administration on (Na K)-ATPase.** Biochemical Pharmacology. 30(1):25-30, 1981.

The effects of lithium, and lithium plus alcohol on (Na K)-adenosine triphosphatase (ATPase) were investigated in rat and goldfish. An increase in alcohol toxicity by lithium and vanadate was evidenced by the marked decrease found in time response to challenge by 3.1% ethanol of goldfish adapted to lithium or vanadate. The maximal effect (approximately 50%) occurred after 2 days exposure to lithium or vanadate, and it diminished with longer exposure. It was found to be reversible after 2 days immersion in tap water. Lithium intake by fish and rats reduces the brain (Na K)-ATPase activity in 2 and 6 days respectively, to one half that of the brains from control animals, but the enzyme level slowly increased to approximately 90% of the original levels during longer periods of treatment. These results and other data indicate that brain (Na K)-ATPase is affected by lithium and alcohol and that these compounds can interact synergistically on the enzyme. 32 references. (Author abstract modified)

002745 Hall, E. D. Program in Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Non-serotonergic depression of spinal monosynaptic reflex trans-**

mission by 5-hydroxytryptophan. Neuropharmacology. 20(2):109-114, 1981.

Intravenous administration of 50mg/kg 5-hydroxytryptophan (5-HTP) to acute unanesthetized spinal cats produced a depression of the lumbar monosynaptic response (MSR) amplitude when the reflex was evoked by supramaximal triceps surae nerve stimulation. The effect of 5-HTP was not antagonized by cincanserin, cyproheptadine, or methyldopa. Amitriptyline not only reversed the effect of 5-HTP on the MSR, it increased the MSR above baseline level. Results indicate that 5-HTP has a depressant action on spinal monosynaptic response transmission that is not related to an increase in spinal serotonergic activity. 13 references. (Author abstract modified)

002746 Hansson, Elisabeth; Jacobson, Ingemar; Venema, Richard; Sellstrom, Ake. Sellstrom: Institute of Neurobiology, University of Goteborg, S-400 33 Goteborg 33, Sweden **Measurement of the membrane potential of isolated nerve terminals by the lipophilic cation (3H)triphenylmethylphosphonium bromide.** Journal of Neurochemistry. 34(3):569-573, 1980.

The use of the lipophilic cation (3H)triphenylmethylphosphonium bromide (TPMP) to measure the membrane potential of synaptosomes was examined. Results showed that TPMP is nontoxic and achieves equilibrium in tissue/medium distribution within a reasonable time of incubation. However, the transport of TPMP was somewhat slow. A membrane potential of about -60mv was calculated in normal incubation conditions. Results indicate that TPMP is a useful tool for monitoring relative changes in the membrane potential of synaptosomal particles, but may not be an adequate measure of the absolute value of the membrane potential. 16 references. (Author abstract modified)

002747 Heath, Robert G.; Fitzjarrell, A. T.; Fontana, C. J.; Garey, R. E. Dept. of Psychiatry and Neurology, Tulane University School of Medicine, 1415 Tulane Avenue, New Orleans, LA 70112 **Cannabis sativa: effects on brain function and ultrastructure in rhesus monkeys.** Biological Psychiatry. 15(5):657-690, 1980.

The effects of marihuana smoking on brain function and ultrastructure were investigated in 21 rhesus monkeys (with and without chronically implanted electrodes). Some monkeys were exposed to smoke of active marihuana, some were administered delta9-tetrahydrocannabinol (delta9-THC), and others were exposed to smoke of inactive marihuana (from which all cannabinols had been removed). To deliver smoke to the monkeys, two different apparatuses were used. Dose schedules comparable to those of human marihuana smokers were established, as determined by plasma levels of delta9-THC. After 2 to 3 months' exposure, the monkeys that were heavy and moderate smokers of active marihuana, and those administered delta9-THC developed chronic recoding changes at deep brain sites, most marked in the septal region, hippocampus, and amygdala. These changes persisted throughout the exposure period (6 or 8 months) and during the postexposure observation period (1 to 8 months). Brains of these electrode implanted monkeys, as well as those without electrodes that were exposed to delta9-THC, showed ultrastructural alterations characterized by changes at the synapse, destruction of rough endoplasmic reticulum, and development of nucleuar inclusion bodies. In contrast, brains of monkeys exposed to smoke of inactive marihuana and of unexposed controls showed no ultrastructural changes. Results indicate that exposure to delta9-THC at doses commensurate with those used by human marihuana smokers can produce permanent alterations in brain function and structure of monkeys. 42 references. (Author abstract modified)

002748 Hedler, Liselotte; Stamm, Georg; Weitzell, Rudolf; Starke, Klaus. Starke: Pharmakologisches Institut, Universitat Freiburg, Hermann-Herder Strasse 5, D-7800 Freiburg i.B., West Germany **Functional characterization of central alpha-adrenoceptors by yohimbine diastereomers.** European Journal of Pharmacology. 70(1):43-52, 1981.

Yohimbine, rauwolscine, corynanthine, tolazoline, and azapetine increased the stimulation evoked overflow of tritium from rat occipital cortex slices preincubated with 3H-noradrenaline, without altering basal overflow. Unlabeled noradrenaline, alpha-methylnoradreline, xylazine, and guanabenz decreased the stimulation evoked overflow of tritium. Pseudoyohimbine and prazosin did not alter evoked overflow in concentrations up to 0.1mcM, but higher concentrations enhanced basal overflow of tritium. In vivo, yohimbine (10mg/kg), rauwolscine (10mg/kg), and corynanthine (10mg/kg) accelerated the alpha-methyltyrosine induced disappearance of noradrenaline from male Wistar rat whole brain. Yohimbine and rauwolscine also accelerated the alpha-methyltyrosine induced depletion of dopamine. 32 references. (Author abstract modified)

002749 Heggli, Dag-Erik; Roed, Asbjorn. Roed: Dept. of Physiology and Biochemistry, Dental Faculty, University of Oslo, P. O. Box 1052, Blindern, Oslo 3, Norway **Diphenylhydantoin-induced block of the rat phrenic nerve-diaphragm preparation pretreated with p-hydroxymercuribenzoate.** European Journal of Pharmacology. 70(2):175-182, 1981.

Pretreatment of the Wistar rat phrenic nerve/diaphragm preparations with the sulfhydryl (SH) blocking agent p-hydroxymercuribenzoate (pOHMB) increased the blocking efficiency of the antiepileptic drug diphenylhydantoin (DPH) during indirect stimulation. The SH blocker N-ethyl-maleimide did not potentiate the block, but SH group protection with dithiothreitol abolished the effect of pOHMB. High calcium concentration potentiated the block which was located at the neuromuscular junction. Microelectrode records in preparations that were curarized, cut, or paralyzed with magnesium to abolish action potential activity revealed an abrupt cessation of end plate potentials (EPPs) after addition of DPH. Pretreatment with pOHMB reduced the time to abrupt EPP fallout in the curarized preparation, suggesting depressed nerve terminal excitability as the cause of the block and its potentiation. Miniature EPPs were observed after EPP cessation, excluding a postsynaptic block. Results suggest that the pOHMB treated preparation is a useful model for testing antiepileptic drugs. 25 references. (Author abstract modified)

002750 Hershkowitz, Norman; Ayala, Giovanni F. Dept. of Neurology, Baylor College of Medicine, Texas Medical Center, Houston, TX 77030 **Effects of phenytoin on pyramidal neurons of the rat hippocampus.** Brain Research. 208(2):487-492, 1981.

The effects of phenytoin on membrane properties and inhibitory postsynaptic potentials (IPSPs) in CA1 and CA3 pyramidal neurons of the in vitro rat hippocampus were examined. No significant change was obsered on input resistance or resting membrane potential. Action potential amplitude, overshoot, rate of rise and rate of decay were decreased. IPSP conductance increase and reversal potential, evoked in CA3 cells through mossy fiber stimulation and in CA1 cells through recurrent and Schaffer's collateral stimulation, were unaffected. 24 references. (Author abstract modified)

002751 Hertting, G.; Zumstein, A.; Jackisch, R.; Hoffmann, I.; Starke, K. Pharmakologisches Institut, Hermann-Herder-Strasse 5, D-7800 Freiburg i. Br., West Germany **Modulation by endogenous dopamine of the release of acetylcholine in the caudate nu-**

cleus of the rabbit. Naunyn-Schmiedeberg's Archives of Pharmacology. 315(2):111-117, 1980.

The electrically evoked release of tritium from slices of rabbit caudate nucleus preincubated with 3H-choline was decreased by apomorphine and increased by haloperidol. Nomifensine and cocaine also reduced the evoked overflow of tritium, and this reduction was antagonized by haloperidol. Pretreatment with reserpine plus alpha-methyl-tyrosine methylester increased the electrically evoked overflow, as did bretyllum. Potassium evoked overflow of tritium was also decreased by apomorphine and increased by haloperidol, and these effects were not altered by tetrodotoxin. Results indicate that striatal dopamine receptors resembling D-2 receptors depress the release of acetylcholine and that some of these receptors are located on cholinergic axon terminals. 27 references. (Author abstract modified)

002752 Hicks, T. P.; Guedes, R. C. A.; Creutzfeldt, O. D. Dept. of Neurobiology, Max Planck Institute for Biophysical Chemistry, Postfach 968, Am Fassberg, D-3400 Gottingen, West Germany **Selective synaptic antagonism by atropine and alpha-aminoadipate of pulvinar and cortical afferents to the suprasylvian visual area (Clare-Bishop area).** Brain Research. 208(2):456-462, 1981.

The synaptic excitations of cells of the Clare/Bishop cortical region produced by electrical stimulation of the pulvinar and ipsilateral cortex, have been shown to be differentially antagonized by iontophoretically applied antagonists. Atropine attenuated the responses evoked by pulvinar stimulation without having an appreciable effect against either iontophoretically applied aspartate or cortically evoked responses. Alpha-aminoadipate antagonized asparate elicited excitations and those obtained with cortical stimulation while leaving unaffected acetylcholine and pulvinar evoked resposes. Results are supportive of the view that acetylcholine and aspartate, or a similar excitatory amino acid, act as synaptic transmitters of some afferents from the pulvinar and ipsilateral cerebral cortex, respectively. 40 references. (Author abstract modified)

002753 Ho, Ing K.; Onoda, Kin-Ichi; Flint, Bryan A. Dept. of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, MS 39216 **Effect of chronic administration of phencyclidine on hepatic mixed-function oxidases in the mouse.** Biochemical Pharmacology. 30(5):545-547, 1981.

The effects of chronic administration of phenycyclidine (PCP) on hepatic drug metabolizing enzymes and several other variables of the multifunction oxidase system were investigated. Two groups of male ICR mice were given PCP or saline for 7 days respectively. Another group of mice was given PCP for 7 days followed by 7 more days at twice the dosage level. The bodyweight gain of mice treated with PCP was reduced significantly. Both the hydroxylation of aniline, pentobarbital, and hexobarbital and the N-demethylation of aminopyrine and ethylmorphine were enhanced significantly in groups 2 and 3. Both reduced nicotinamide adenine dinucleotide phosphate (NADPH) dehydrogenase and NADPH-cytochrome-c reductase activities were also increased. Cytochrome P-450 and cytochrome-b5 content, however, were less affected. It is concluded that chronic administration of a high dose of PCP enhances the hepatic drug metabolizing enzyme systems. 29 references.

002754 Homan, Harvey D.; Ziance, Ronald J. Dept. of Pharmaceutical Science, College of Pharmacy and Allied Health, St. John's University, Jamaica, NY 11439 **The effects of d-amphetamine and potassium on serotonin release and metabolism in rat cerebral cortex tissue.** Research Communications in Chemical Pathology and Pharmacology. 31(2):223-240, 1981.

Potassium (K) evoked release of tritiated serotonin (3H-5 HT) from chopped male Sprague-Dawley rat cerebral cortex preincubated with 3H-5 HT was dependent on calcium, but 3H-5 HT release induced by d-amphetamine was not calcium dependent. Potassium also caused a significant increase in the percentage of 3H-5-hydroxyindoleacetic acid (3H-5HIAA) released from the tissue. Incubation with fluoxetine, a selective 5 HT uptake inhibitor, did not alter the increased 3H-5 HIAA formation induced by potassium. Results suggest that d-amphetamine and potassium release 3H-5 HT by different mechanisms. 16 references. (Author abstract modified)

002755 Homma, Shinji. Dept. of Physiology, Faculty of Medicine, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan **Depression of ventral root-dorsal root potential by DL-alpha-aminoadipate in frog spinal cord.** Brain Research. 208(1):240-243, 1981.

The depression of ventral root dorsal root potential (VR/DRP) by DL-alpha-aminoadipate (DL-alpha-AAD) in isolated hemisectioned frog spinal cord is reported. It is suggested that acidic amino acid receptors might be subserving for the generation of VR/DRP in addition to the initial cholinergic link between motoneurons and interneurons and the electrical coupling between motoneurons and primary afferent terminals and the 1st step between unidentified interneurons and primary afferent terminals which had been reported to be mediated by GABA. 14 references. (Author abstract modified)

002756 Huidobro-Toro, J. Pablo; Miranda, H.; Huidobro, F. Dept. of Pharmacology, University of California, San Francisco Medical Center, San Francisco, CA 94143 **Development of tolerance to the excitatory effect of morphine and cross-tolerance to the inhibitory action of beta-endorphin in the isolated rat vas deferens.** Life Sciences. 28(7):773-779, 1981.

The development of tolerance to the excitatory effect of morphine and cross-tolerance to the inhibitory action of beta-endorphin were studied in the isolated rat vas deferens. Morphine caused an increase in the neuromuscular twitch evoked by electrical stimulation. In rats chronically treated with morphine, the concentration of the opiate required to cause a 50% increase in the twitch was about three times larger than needed to elicit the same response in vasa from rats treated with a placebo. The simultaneous administration of naloxone plus morphine partially antagonized tolerance development by about 22%. Morphine tolerance was extended to other opiate like alkaloids such as etonitazene and a derivative of azidomorphine. In contrast to the effects of morphine, beta-endorphin inhibited neuromuscular transmission. Vasa from rats chronically treated with morphine were about 10 times less sensitive to the inhibitory effect of beta-endorphin as compared to paired placebo treated controls. Chronic naloxone treatment in conjunction with morphine significantly reduced the cross-opiate tolerance by 66%. Results suggest that morphine may interact at two different sites in the nerve terminals of the rat vas deferens. 24 references. (Author abstract modified)

002757 Huidobro-Toro, J. Pablo; Way, E. Leong. Dept. of Pharmacology, University of California, San Francisco, San Francisco, CA 94143 **Comparative study on the effect of morphine and the opioid-like peptides in the vas deferens of rodents: species and strain differences, evidence for multiple opiate receptors.** Life Sciences. 28(12):1331-1336, 1981.

The effects of an opiate alkaloid and an opioid like peptide were studied on the electrically evoked twitching of the vas deferens of three common laboratory rodents. Normorphine and the synthetic opioid peptide D-Alanine2 methionine enkephalinamide (D-Ala2) produced dose dependent inhibitions of the twitching response in the mouse vas deferens. In the rat vas deferens, while beta-endorphin caused an inhibitory effect in three strains of rats to a similar degree, morphine produced a dose related enhancement of the twitching. In the guinea-pig, both morphine and beta-endorphin caused an increase in the muscular twitch. Results are interpreted in terms of an heterogeneous mixture of opiate receptors present in the vas deferens from these rodents. The mouse appears to contain mainly delta receptors while the rat has mostly epsilon receptors characterized by their specificity and sensitivity to the action of beta-endorphin. The guinea-pig vas deferens had apparently lost the sensitivity to the inhibitory influence of the opioids, suggesting the absence of mu or delta opiate receptors in this tissue. 18 references. (Author abstract)

002758 Hurd, Russell W.; Hammond, Edward J.; Wilder, B. J. Dept. of Neuroscience, College of Medicine, University of Florida, Gainesville, FL 32610 **Homocysteine induced convulsions: enhancement by vitamin B6 and inhibition by hydrazine.** Brain Research. 209(1):250-254, 1981.

The effects of pyridoxal phosphate, pyridoxine, and hydrazine were studied on homocysteine induced seizures in mice. Both of the B6 vitamers significantly decreased the latency and increased the severity, lethality, and duration of seizures induced by homocysteine. The B6 inhibitor hydrazine sulfate, which is normally a convulsant, prevented the tonic component of the convulsions and increased the latency of the clonic component. Results indicate that a vitamin B6 dependent step is critically involved in the metabolic changes which precede homocysteine seizures. 25 references. (Author abstract)

002759 Hutchinson, Ronald R.; Emley, Grace S. Foundation for Behavioral Research, Augusta, MI 49012 **Nicotine ingestion reduces elevated blood pressures in rats and squirrel monkeys.** Life Sciences. 28(7):801-809, 1981.

The effects of nicotine tartrate added to the home cage drinking water of albino rat and squirrel monkey Ss on blood pressure and behavior were investigated. All Ss receiving nicotine showed reduced blood pressure elevations to noxious stimulation compared to water control Ss, and these reductions were greater at higher drug doses. Squirrel monkeys having high blood pressures showed dose dependent blood pressure decreases, whereas Ss possessing low resting pressures demonstrated little or no blood pressure change during drug intake. Upon termination of drug intake, pressures rapidly increased to predrug levels. Results are concordant with previous studies demonstrating that oral nicotine ingestion causes reductions in aggressive behavior, and suggest that nicotine is selectively influential in altering the biological state of anger, decreasing both its behavioral and somatic components. 34 references. (Author abstract modified)

002760 Hyttel, John. Dept. of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **Similarities between the binding of 3H-piflutixol and 3H-flupentixol to rat striatal dopamine receptors in vitro.** Life Sciences. 28(5):563-569, 1981.

The binding of a tritium labelled thioxanthene neuroleptic, piflutixol, to rat striatal membranes in vitro has been characterized. Neuroleptics were found to inhibit the binding of 3H-piflutixol, 3H-flupentixol, and 3H-haloperidol as well as the dopamine (DA) stimulated adenylate cyclase activity. A detailed analysis of the inhibition of 3H-piflutixol binding by haloperidol and apomorphine revealed two classes of 3H-piflutixol binding sites. It is concluded that 3H-piflutixol binds predominantly to the same class of DA receptors as does 3H-flupentixol. This class, D1 receptors, is associated with acetylcholine activity and is distinct from those labelled by 3H-haloperidol. 14 references. (Author abstract modified)

002761 Idenoue, Junzo. Dept. of Neuropsychiatry, Faculty of Medicine, Kagoshima University, Kagoshima, 890 Japan **Chronological electroencephalographic and neuropharmacological study in cortical kindling rabbits.** Kyushu Neuro-Psychiatry. 25(3-4):191-211, 1979.

Electroencephalographic and behavioral developments in cortical kindling in rabbits were studied chronically; postkindling influences of some drugs on afterdischarge (AD) duration and behavioral changes were tested. Four stages were observed in behavioral development: 1) adversive seizure; 2) adversive seizure with facial twitching; 3) adversive seizure with loss of postural control; and 4) generalized seizure with sudden loss of postural control. AD duration increased progressively, especially after the fourth stage, when waveforms also were changed greatly. Independent interictal discharges (IID) were seen on completion of kindling, especially at the mirror regions. Mutual dependency of EEG activities between the primary focus and the mirror focus was observed after kindling. Diphenylhydantoin, phenobarbital, and diazepam suppressed AD durations and seizures; as did GABOB and sodium valproate but to a lesser degree. L-dopa was ineffective. The low dose of oxyperitine suppressed AD durations, while the high dose of the oxypertine provoked seizure. Eserine and atropine also were examined. The kindling effect as a model of epilepsy makes it possible to screen test potential anticonvulsants. 99 references. (Author abstract modified)

002762 Ientile, R.; Di Giorgio, R. M.; Rotiroti, D.; Nistico, G. Institute of Biochemistry, Faculty of Medicine, University of Messina, Messina, Italy **GABA depletion in chick brain-stem after intraventricular injection of cefazolin.** Research Communications in Chemical Pathology and Pharmacology. 31(2):241-250, 1981.

Injections of cefazolin into the third cerebral ventricle of young chicks caused a dose dependent fall in GABA content in the brainstem. The GABA decrease was evident within 15 minutes, reached its nadir at 60 minutes, and disappeared within 120 minutes. Glutamate decarboxylase and GABA-transaminase activities were not significantly altered. Results suggest that the excitatory and convulsant effects of cefazolin in chicks are related to GABA depletion in the brainstem. 29 references. (Author abstract modified)

002763 Jahnsen, Henrik; Laursen, Arne Mosfeldt. University of Copenhagen, Panum Institute, Institute of Neurophysiology, Blegdamsvej 3 C, DK-2200, Copenhagen N, Denmark **The effects of a benzodiazepine on the hyperpolarizing and the depolarizing responses of hippocampal cells to GABA.** Brain Research. 207(1):214-217, 1981.

The effects of a benzodiazepine on the hyperpolarizing and the depolarizing responses of guinea-pig hippocampal cells to GABA were investigated. Application of GABA in the pyramidal layer close to the impaled cell produced a hyperpolarization. Applied in the stratum radiatum, penetrations of the GABA electrode along a line normal to the pyramidal cell layer produced a depolarizing response. Occasionally, both responses were obtained in sequence beginning with hyperpolarization. This biphasic response was obtained when the tip of the GABA electrode was placed 50 mcm or less from the pyramidal layer. The functional significance of the depolarizing response as well as its enhancements by midazolam are discussed. 11 references.

002764 James, J. Howard; Fischer, Josef E. Dept. of Surgery, University of Cincinnati Medical Center, Cincinnati, OH 45267

Transport of neutral amino acids at the blood-brain barrier. Pharmacology. 22(1):1-7, 1981.

The movement of neutral amino acids across the blood-brain barrier is discussed. Available evidence points to the existence of a single transport system at the luminal capillary surface. Experimental data suggest that amino acid influx is coupled to efflux, particularly efflux of glutamine synthesized in glial astrocytes from ammonia and glutamic acid. Such a coupling could account for increased blood-brain neutral amino acid transport in liver disease and decreased transport activity after treatment with methionine sulfoximine, a glutamine synthetase inhibitor. 40 references. (Author abstract modified)

002765 Janka, Z.; Szentistvanyi, I.; Joo, F.; Juhasz, A.; Rimanoczy, A. Dept. of Neurology, University Medical School, Szeged, Hungary **Effects of lithium on morphological characteristics of dissociated brain cells in culture.** Acta Neuropathologica. 46:117-121, 1979.

Lithium chloride was added in 5 and 10 mM concentrations for different periods of time to dissociated cultures obtained from chicken embryonic brain. Addition of lithium at day 1 in vitro for 5 days resulted in a dose dependent decrease in total protein in the cultures as compared to sodium treated controls. A profound reduction was revealed in the length of neuronal processes and in the number of neuronal cell bodies by phase contrast and morphometric means. After exposure to lithium in 10 mM concentration for 48 hours, a slight decrease in the number of perikaryons and a marked reduction in process length of neural elements was observed in the 6-day-old tissue cultures. Ultrastructurally, swollen and degenerating nerve processes have been found after lithium treatment suggesting a particular sensitivity of these structures to the lithium ion. (Journal abstract)

002766 Johnson, Kenneth M.; Oeffinger, Kevin C. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **The effect of phencyclidine on dopamine metabolism in the mouse brain.** Life Sciences. 28(4):361-369, 1981.

The effect of phencyclidine (PCP) on dopamine (DA) metabolism in the mouse brain was investigated. Administration of PCP to mice resulted in no change in brain levels of tyrosine, DA, norepinephrine (NE), or homovanillic acid (HVA). Although PCP reduced plasma tyrosine levels, no effect of PCP on the utilization of DA or NE after blockade of synthesis with alpha-methyl-p-tyrosine (AMPT) was observed. In addition, PCP did not affect the probenecid induced accumulation of HVA. However, PCP was observed to potentiate the haloperidol induced increase in HVA concentration, and the haloperidol induced decline in DA levels after AMPT. The former effect was blocked by baclofen, suggesting that PCP mobilizes DA for impulse dependent release. This effect could not be attributed to an antagonism of presynaptic DA receptors. These effects are similar to those of the nonampehtamine stimulant class of drugs. 47 references. (Author abstract modified)

002767 Johnson, S. M.; Duggan, A. W. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, Australia **Evidence that the opiate receptors of the substantia gelatinosa contribute to the depression, by intravenous morphine, of the spinal transmission of impulses in unmyelinated primary afferents.** Brain Research. 207(1):223-228, 1981.

Evidence that the opiate receptors of the substantia gelatinosa contribute to the depression, by intravenous morphine, of the spinal transmission of impulses in unmyelinated primary afferents is described. In barbiturate anesthetized cats, dorsal horn neurons were excited by electrical stimulation of the common tibial nerve. The numbers of action potentials evoked by excitation of C-fibers were depressed by analgesic doses of morphine. Naloxone, administered electrophoretically in the substantia gelatinosa, fully reversed the inhibitory action of morphine. Results suggest that opiate receptors in the substantia gelatinosa play a role in morphine analgesia. 18 references. (Author abstract modified)

002768 Johnston, G. A. R.; Lodge, D.; Bornstein, J. C.; Curtis, D. R. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, A.C.T., 2600 Australia **Potentiation of L-glutamate and L-aspartate excitation of cat spinal neurones by the stereoisomers of threo-3-hydroxyaspartate.** Journal of Neurochemistry. 34(1):241-243, 1980.

Threo-3-hydroxy-L-aspartate (THLA) and its stereoisomer threo-3-hydroxy-D-aspartate (THDA) potentiated the excitation of cat spinal neurons by excitants that are taken up actively by the CNS, including L-glutamate, L-aspartate, and D-glutamate. THLA and THDA did not alter excitation by acetylcholine, kainate, and N-methyl-D-aspartate. Results suggest that uptake processes sensitive to THLA and THDA are important for the maintenance of low extracellular concentrations of the excitatory transmitters L-glutamate and L-aspartate. 15 references.

002769 Johnston, G. A. R.; Willow, M. Dept. of Pharmacology, University of Sydney, New South Wales, 2006, Australia **Barbiturates and GABA receptors.** Advances in Biochemical Psychopharmacology. 26:191-198, 1981.

A dose dependent enhancement of GABA binding by pentobarbital which involves an increased affinity of GABA for the higher affinity of the two apparent binding sites is reported in a membrane preparation designed to preserve interaction between endogenous inhibitors and GABA binding sites. The discrepancy between these results and previous studies of the effect of pentobarbital on high affinity GABA binding is attributed to the membrane preparations employed. It is noted that the concentrations of pentobarbital which enhance GABA binding are comparable with those measured in the brain during surgical anesthesia in laboratory animals. 24 references.

002770 Johnston, M. V.; Carman, A. B.; Coyle, J. T. Coyle: Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Effects of fetal treatment with methylazoxymethanol acetate at various gestational dates on the neurochemistry of the adult neocortex of the rat.** Journal of Neurochemistry. 36(1):124-128, 1981.

The effects of gestational date (13, 14, 15, and 17 days) of administration of methylazoxymethanol acetate (20mg/kg) on the cortical synaptic chemistry and morphology of the rat was examined in adult offspring. Treatment at 13 days of gestation (DG) resulted in cortical hypoplasia that affected primarily the deep layers whereas treatment at 14 and 15 days gestation caused a severe hypoplasia of cortical neurons above layer V and a 66% to 77% reduction in cortical mass. The 17 DG treatment caused only a 20% reduction in cortical weight with effects apparent only in the superficial layers. At no treatment date did the specific activity of glutamate decarboxylase differ significantly from control. In contrast, presynaptic markers for nonradrenergic (tyrosine hydroxylase and norepinephrine) and for serotonergic (serotonin) terminals were increased in concentration in direct proportion to the degree of cortical hypoplasia. The specific activity of choline acetyltransferase was significantly increased at all treatment dates, but total activity per cortical slab was significantly reduced on treatment days 13 to 15. 17 references. (Author abstract)

002771 Kameyama, Tsutomu; Nabeshima, Toshitaka; Yoshida, Naoyuki; Yamaguchi, Kazumasa. Nabeshima: Dept. of Pharmacology and Toxicology, University of Mississippi Medical Center, 2500 North State St., Jackson, MS 39216 **Neurochemical studies of an analgesic, 1,3-diphenyl-5-(2-dimethylaminopropionamide)-pyrazole (difenamizole).** Research Communications in Chemical Pathology and Pharmacology. 31(1):31-53, 1981.

Studies in male ddy mice indicated that difenamizole (DFZ) may exert its analgesic activity by inhibiting the release of dopamine (DA) and preventing the binding of DA to receptors. DFZ enhanced the accumulation of DA in the striatum after pargyline. The analgesic also inhibited the following: the binding of 3H-DA to striatal synaptic membranes, the uptake of DA by striatal synaptosomes, and the potassium evoked release of DA in striatal slices. DFZ inhibited monoamine oxidase activity, but did not alter catechol-0-methyltransferase activity. 29 references. (Author abstract modified)

002772 Kamp, Cylia W.; Morgan, William W. Dept. of Anatomy, University of Texas Health Science Center, San Antonio, TX 78284 **GABA antagonists enhance dopamine turnover in the rat retina in vivo.** European Journal of Pharmacology. 69(3):273-279, 1981.

Retinal dopamine turnover in dark adapted male Sprague-Dawley rats was stimulated by intraocular injections of the GABA antagonists picrotoxin and bicuculline methiodide. Atropine pretreatment did not alter this effect. Results suggest that endogenous GABA tonically inhibits dopamine neurons in the dark adapted rat retina. This inhibition appeared to be reduced by exposure to light. 25 references. (Author abstract modified)

002773 Kaneno, Shigeru. Dept. of Neuropsychiatry, School of Medicine, Tokyo Medical and Dental University, Tokyo, Japan **Effects of chlorpromazine on dopaminergic receptor functions in rat brain -- difference of the response of several dopaminergic systems after chronic administration.** Psychiatria et Neurologia Japonica. 82(6):335-352, 1980.

The effects of chlorpromazine on dopamine receptor functions in several rat brain regions were investigated. Ss were adult male Wistar rats. The results of acute treatment indicate that chlorpromazine competitively inhibited dopamine receptors in all brain areas, while 3H-spiroperidol binding activity and dopamine sensitive adenylate cyclase activity showed that dopamine receptor sensitivity increased in the nigrostriatal system but not in the mesocortical system or in some areas of the mesolimbic system. The results indicate that tolerance to extrapyramidal side-effects develops in the early stages of treatment and that antipsychotic drugs have continued blocking effects on dopamine receptors in the mesocortical system and in a part of the mesolimbic system. 45 references. (Author abstract modified)

002774 Karlsen, R. Lund; Grofova, I.; Malthe-Sorenssen, D.; Fonnum, F. Fonnum: Norwegian Defence Research Establishment, Division for Toxicology, P.O. Box 25, N-2007 Kjeller, Norway **Morphological changes in rat brain induced by L-cysteine injection in newborn animals.** Brain Research. 208(1):167-180, 1981.

Morphological changes in rat brain induced by L-cysteine injection in newborn animals are described. A single subcutaneous injection of L-cysteine to rats on postnatal day 4 was followed by atrophy of the brain which was well developed 27 to 32 days after the injection. It is apparent that the lesioned animals can be divided into two groups: 1) in type 1 (80% of Ss), bodyweight was unchanged, but total brain weight was reduced by about 20%; and 2) in type 2 there was a 50% reduction in wet weight of brain and bodyweight. In type 2 (10% of the survivors), the cortex and the hippocampus were reduced by 80% and 60% respectively. In this type of lesion, significant morphological changes were observed in several brain regions such as the caudato/putamen, thalamus, pons, medulla oblongata, spinal cord, and cerebellum. 18 references. (Author abstract modified)

002775 Karobath, Manfred; Drexler, Gerhard; Supavilai, Porntip. Dept. of Biochemical Psychiatry, Psychiatrische Universitatsklinik, A-1090 Vienna, Austria **Modulation by picrotoxin and iptbo of 3H-flunitrazepam binding to the GABA/benzodiazepine receptor complex of rat cerebellum.** Life Sciences. 28(3):307-313, 1981.

The modulation by picrotoxin and IPTBO of 3H-flunitrazepam binding to the GABA benzodiazepine receptor complex of rat cerebellum was investigated. The actions of these two drugs on 3H-flunitrazepam binding to membranes from rat cerebellum include: 1) both drugs in high concentrations stimulate 3H-flunitrazepam binding mainly by increasing the apparent number of binding sites; this effect is chloride ion dependent and reversible; 2) they inhibit 3H-flunitrazepam binding stimulated by the pyrazolopyridine etazolate (SQ 20009), and this effect is observed in binding experiments performed at low and at physiological temperature; 3) they inhibit GABA stimulated binding in a chloride ion dependent mode. This action is much more potent when the binding experiments are performed at physiological temperatures. These results demonstrate that drugs which act on GABA receptor associated chloride ion channels have potent modulatory effects on benzodiazepine receptor binding in cerebellum. 20 references. (Author abstract modified)

002776 Keeton, T. Kent; Krutzsch, Henry; Lovenberg, Walter. Dept. of Pharmacology, University of Texas Health Science Center, San Antonio, TX 78284 **Specific and sensitive radioimmunoassay for 3-methoxy-4-hydroxyphenylethyleneglycol (MOPEG).** Science. 211(4482):586-588, 1981.

Antibodies that specifically bind the norepinephrine metabolite 3-methoxy-4-hydroxyphenylethyleneglcycol (MOPEG) were produced in rabbits after injection of a derivative of MOPEG conjugated with bovine thyroglobulin. A sensitive radioimmunoassay was devised with this antiserum in which as little as 0.5 nanogram of MOPEG can be accurately measured with a final antibody dilution of 1 to 180. The antibody appears to be specific for MOPEG, since tritiated MOPEG was not displaced from the antibodies by norepinephrine, epinephrine, dopamine, serotonin, or their major metabolites, including MOPEG sulfate (333 nanograms each). 20 references. (Author abstract)

002777 Kelley, Keith W. Dept. of Animal Sciences, Washington State University, Pullman, WA 99164 **Lithium, assimilation of nutrients and reproduction. (Unpublished paper).** Final Report, NIMH Grant R01-MH-32812, 1980. 7 p.

The effects of dietary lithium on ovulation rate and embryo mortality, gastrointestinal physiology, and aggressive behavior were investigated. Experiments with female pigs showed that there were no differences among treatments in the length of the estrous cycle, the number of breedings per gilt, the number of corpora lutes, ovarian weight, the number of live embryos, the number of dead embryos, or overall embryo viability. These data suggest that reproductive function in manic-depressive female patients may not be compromised. Even though the data on absorption of glucose in young pigs were confounded partially by feed intake, no obvious differences in energy metabolism or gastrointestinal function were noted. The data confirmed that injectable lithium reduces shock induced aggression in rats and that this antiaggressive effect is removed when the area postrema is lesioned. It was found that area postrema lesions abolish the ability of lithium to condition taste aversions. 4 references.

002778 Kendall, David A.; Stancel, George M.; Enna, S. J. Enna: Dept. of Anatomy, University of Texas Medical School, Houston,TX 77025 **Imipramine: effect of ovarian steroids on modifications in serotonin receptor binding.** Science. 211(4487):1183-1185, 1981.

The effect of ovarian steroids on imipramine induced changes in serotonin receptor binding were studied in female Sprague-Dawley rats. Long-term administration of imipramine caused a decrease in serotonin-2 receptor binding in rat brain cerebral cortex, an effect that was abolished by ovariectomy. In contrast, ovariectomy had no effect on imipramine induced decreases in hippocampal serotonin or in cerebral cortical and hippocampal beta-adrenergic receptor binding. Administration of estradiol or progesterone separately or in combination reestablished the effect of imipramine treatment on cortical serotonin-2 receptors. These results suggest that ovarian steroids may play an important, but subtle, role in the neurochemical and perhaps clinical response to this antidepressant drug. 17 references. (Author abstract modified)

002779 Kennett, G. A.; Joseph, M. H. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England **The functional importance of increased brain tryptophan in the serotonergic response to restraint stress.** Neuropharmacology. 20(1):39-43, 1981.

The increase in brain tryptophan induced by restraint stress in rats was shown to be prevented by prior administration of valine, 200mg/kg (i.p.). Brain 5-hydroxytryptamine (5-HT) was not depleted, but the stress induced increase in 5-hydroxyindoleacetic acid (5-HIAA) was prevented. A 5-HT mediated functional response to stress, elevated plasma corticosterone was, however, significantly attenuated by valine pretreatment, but was not affected by valine treatment alone. This suggests that the increase in 5-HIAA in brain is not merely secondary to increased brain tryptophan, but indicates an increase in functional 5-HT activity, which is in turn at least partly dependent on the increase in brain tryptophan. Measurement of kynurenine levels in the same animals indicated an increase in synthesis in stress, but did not support the hypothesis that competition occurs between the kynurenine and 5-hydroxyindole pathways of tryptophan metabolism in brain. 30 references. (Author abstract modified)

002780 Kesner, Raymond P.; Partlow, Lester M.; Bush, Lloyd G.; Berman, Robert F. Dept. of Psychology, University of Utah, Salt Lake City, UT **A quantitative regional analysis of protein synthesis inhibition in the rat brain following localized injection of cycloheximide.** Brain Research. 209(1):159-176, 1981.

Inhibition of protein synthesis following bilateral injection of cycloheximide (CHX) was quantified in various brain regions of rats (amygdala, internal capsule, caudate, cortex, hippocampus, thalamus, hypothalamus and the entire half brain). Regional inhibition of protein synthesis was determined by analysis of autoradiograms from different brain levels using an image analyzing computer to measure the optical densities of microscopic areas corresponding to discrete neuroanatomical structures. Since injection of CHX into the amygdala resulted in a profound inhibition of protein synthesis in both the amygdala and internal capsule while injection into the internal capsule only caused a marked inhibition in the capule itself, these results provide a possible explanation for the observation that injection of CHX into the amygdala produced a retention deficit while injection into the adjacent internal capsule had no effect on memory function. Amygdaloid function rather than brain functioning in general is implicated in the CHX induced impairment of memory. 13 references. (Author abstract modified)

002781 Kim, Jang-Soo; Uchimura, Hideyuki; Hirano, Makoto; Saito, Masashi; Matsumoto, Takashi; Nakahara, Tatsuo. Laboratory of Neurochemistry, Hizen National Mental Hospital, Kanzaki, Saga, 842-01, Japan **Type B monoamine oxidase activities toward beta-phenylethylamine in discrete hypothalamic and circumventricular nuclei of the rat.** Biochemical Pharmacology. 30(8):893-895, 1981.

Type-B monoamine oxidase (MAO) activities toward beta-phenylethylamine (PEA) in discrete hypothalamic and circumventricular nuclei of the rat were studied in freeze dried sections using radiochemical micromethods. Of the hypothalamic nuclei and circumventricular regions examined, PEA/MAO activities varied about five fold between the regions with the highest and the lowest values. The highest activities were found in the posterior part of the nucleus arcuatus; the nucleus hypothalamicus anterior, the nucleus hypothalamicus posterior, and the medial part of the lateral hypothalamic area had low PEA/MAO activities. Results indicate directly that the circumventricular regions or nuclei are generally rich in type-B MAO and that an active metabolism of PEA, or of other endogenous monoamines specific for type-B MAO, may occur in those regions. 23 references.

002782 King, W. Michael; Kreisman, Norman R. Kreisman: Dept. of Physiology, Tulane University School of Medicine, New Orleans, LA 70112 **Trimethadione effects on cholinergic responses in Aplysia neurons.** Brain Research. 209(1):221-226, 1981.

The anticonvulsant, trimethadione (TMO), was tested for effects on cholinergic responses to iontophoretic application of acetylcholine on identified neurons in Aplysia. TMO (1 to 10mM) depressed the amplitudes of depolarizing responses mediated by Na and hyperpolarizing responses mediated by Cl- but did not affect hyperpolarizing responses mediated by K. Such a combination of effects on cholinergic responses distinguishes the action of this antiabsence drug from agents effective against tonic/clonic seizures and from convulsant drugs. 18 references. (Author abstract)

002783 Kitchen, Ian; Hart, Stephen L. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, Turner St., London E1 2AD, England **Differential loss of biological activity of the enkephalins induced by current.** European Journal of Pharmacology. 69(3):393-396, 1981.

Passage of current across solutions of enkephalins caused a loss of biological activity of the peptides proportional to the strength of the current. The presence of a mouse vas deferens prevented the current induced loss of activity of leu-enkephalin, but had no effect on the loss of activity of met-enkephalin. These results may account for the differential potency of the enkephalins on the vas and for the inability of several laboratories to show electrically induced enkephalin release. 10 references. (Author abstract modified)

002784 Kleshchinov, V. N. Laboratoriya eksperimental'noy patologii i patomorfologii mozga Instituta Psikhiatrii AMN SSSR, Moskva, USSR **/Changes in the cortical activity of succinate dehydrogenase under the influence of chlorpromazine (a histochemical and electrocytochemical study)./** Izmeneniya aktivnosti suktsinatdegidrogenazy v kore golovnogo mozga pod vliyaniyem aminazina (gistokhimicheskoye i elektronno-tsitokhimicheskoye issledovaniye). Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(7):1024-1027, 1980.

The activity and location of succinate dehydrogenase (SDH) in the cortex of the brains of rats were studied before and after the administration of chlorpromazine in the amount of 15 mg/kg. Changes in the enzyme activity according to photometry occurred in two ways: a general decrease in the activity of neurons and neuropil, and a decrease in the number of neurons reacting to SDH. Ultrastructurally the enzyme was detectable in the mitochondria of the cell body, adjacent processes and in the processes of cells surrounding the blood vessels. In most of the neuropil mitochondria the produce of the reaction was not found. Under the influence of chlorpromazine dark neurons appeared lacking organelles containing products of reaction. There were also light neurons in the mitochondria without products of reaction, and lipofucsin granules containing products of reaction. Results explain the drop in the SDH activity, found during photometry of histochemical changes. 11 references. (Journal abstract modified)

002785 Koch, Kevin M.; Ludwick, B. Teri; Levy, Rene H. Levy: Dept. of Pharmaceutics, School of Pharmacy, Bagley Hall BG-20, University of Washington, Seattle, WA 98195 **Phenytoin -valproic acid interaction in rhesus monkey.** Epilepsia. 22(1):19-25, 1981.

The interaction between phenytoin (PHT) aad valproic acid (VPA) was investigated in the rhesus monkey. PHT was given by multiple IV bolus to reach a steady-state and then continued while two successive VPA infusions were added. Plasma was assayed for total VPA and PHT as well as free PHT. The addition of VPA produced no change in total PHT levels, a 50% increase in PHT free fraction (increase in free PHT levels), and a decrease in PHT overall elimination rate constant. The increase in free fraction was also documented in a separate in vitro study. The increase in free PHT levels suggested that VPA decreased PHT intrinsic metabolic clearance. This interaction may thus involve a dual mechanism, protein binding displacement of PHT and inhibition of PHT metabolism. This mechanisms is compatible with other studies showing that VPA is an ihibitor of drug metabolism. 27 references. (Author abstract modified)

002786 Koe, B. Kenneth. Dept. of Pharmacology, Central Research, Pfizer Inc., Groton, CT 06340 **Levonantradol, a potent cannabinoid-related analgesic, antagonizes haloperidol-induced activation of striatal dopamine synthesis.** European Journal of Pharmacology. 70(2):231-235, 1981.

Levonantradol antagonized the compensatory acceleration of striatal dopamine synthesis induced by haloperidol in male Sprague-Dawley rats. The enantiomer dextronantradol was 30 times less effective. The haloperidol effect was also attenuated by delta9-tetrahydrocannabinol, but at a dose 320 times higher than levonantradol; cannabidiol was inactive at a dose 750 times higher. GABA like actions of levonantradol may be responsible for the antagonism of haloperidol, but anticholinergic effects may also contribute. 14 references. (Author abstract modified)

002787 Koide, T.; Matsushita, H. Dept. of Pharmacology, Research Labs. of Chugai Pharmaceutical Co. Ltd., No. 41-8, 3-chome, Takada, Toshima-ku, Tokyo, Japan **Influence of a chronic new potential antidepressant, 1-(3-(dimethylamino)propyl) 5-methyl-3-phenyl-1H-indazole (FS32) and its N-desmethylated compound (FS97): treatment on monoaminergic receptor sensitivity in the rat brain.** Neuropharmacology. 20(3):285-292, 1981.

The effects on male Sprague-Dawley rat brain monoaminergic receptor binding of the potential antidepressants 1-(3-(dimethylamino)propyl)-5-methyl-3-phenyl-1H-indazole (FS32) and its N-desmethylated compound (FS32) were compared with those of the classical tricyclic antidepressants, imipramine and desipramine. Single injections of these four drugs did not alter specific binding to beta-adrenergic, serotonergic, and dopaminergic receptors. Chronic treatment with each drug for 4 weeks significantly decreased specific binding to beta-adrenergic receptors and dopaminergic receptors, but not to serotonergic receptors. Results suggest that the beta-adrenergic and dopaminergic receptor subsensitivity induced by chronic treatment with FS32 or FS97 may play a role in their antidepressant actions. 48 references. (Author abstract modified)

002788 Koide, T.; Matsushita, H. Dept. of Pharmacology, Research Laboratories of Chugai Pharmaceutical Co., Ltd., No. 41-8, 3-chrome, Takada, Toshima-ku, Tokyo, Japan **An enhanced sensitivity of muscarinic cholinergic receptor associated with dopaminergic receptor subsensitivity after chronic antidepressant treatment.** Life Sciences. 28(10):1139-1145, 1981.

The chronic effects of antidepressant treatment of striatal dopaminergic (DA) and muscarinic cholinergic (mACh) receptors of the rat brain was examined comparatively using 3H-spiroperidol (3H-SPD) and 3H-quinuclidinyl benzilate (3H-QNB) as the radioactive ligands. Imipramine and desipramine were used as prototype antidepressants. Although a single administration of imipramine or desipramine did not affect each receptor sensitivity, chronic treatment with each drug caused a supersensitivity of mACh receptor subsequent to DA receptor subsensitivity. Furthermore, it has been suggested that anti-mACh properties of imipramine or desipramine may not necessarily be related to the manifestation of mACh receptor supersensitivity and that sustained DA receptor subsensitivity may play some role in the alterations of mACh receptor sensitivity. 39 references. (Author abstract)

002789 Kolbe, H.; Clow, A.; Jenner, P.; Marsden, C. D. Marsden: University Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London SE5, England **Neuroleptic-induced acute dystonic reactions may be due to enhanced dopamine release on to supersensitive postsynaptic receptors.** Neurology. 31(4):434-439, 1981.

The temporal relationship between increased dopamine synthesis and release and the change in postsynaptic dopamine receptor sensitivity in rats given a single dose of the phenothiazine butaperazine was investigated. Oral administration of butaperazine (40mg/kg) to rats increased dopamine turnover, as measured by elevation of striatal and mesolimbic concentrations of homovanillic acid and 3,4-dihydroxyphenylacetic acid, for 24 to 48 hours. Initially, this dose of butaperazine inhibited stereotyped behavior in response to subcutaneous administration of apomorphine, but this effect was reversed at 12 hours. Later, animals had normal or exaggerated responses to apomorphine. The data suggest that at the critical 20 to 28 hour period after butaperazine administration, when most human dystonic reactions occur, normal or supersensitive cerebral dopamine receptors are exposed to an excessive synaptic release of dopamine. This may be responsible for the drug induced dystonia. 25 references. (Author abstract modified)

002790 Komissarov, I. V.; Abramets, I. I. Donetskiy gosudarstvennyy meditsinskiy institut im. A. M. Gor'kogo, Donetsk, USSR **/The effect of monoamines on motoneurons of the isolated rat spinal cord./** Vliyaniye monoaminov na motoneyrony izolirovannogo spinnogo mozga krysy. Neyrofiziologiya. 12(4):391-396, 1980.

The effect of monoamines on motoneurons of the isolated rat spinal cord was studied. Results show that superfusion of isolated hemisected rat spinal cord by a solution containing noradrenaline induces depolarization or hyperpolarization of motoneurons, depending on amine concentrations. Both effects are due to the direct influence of amine on motoneurons, since they remain in the medium with an abundance of Mg ions and a deficit of Ca ions. Both depolarization and hyperpolarization of motoneurons induced by noradrenaline are depressed by alpha-adrenoblockers. Depolarization of motoneurons induced by dopamine is suppressed in the medium with an abundance of Mg ions. Hyperpolarization of motoneurons induced by dopamine is suppressed by the addition of haloperidol, but remains unchanged when phentolamine is added. Depolarization of motoneurons induced by serotonin and its metabolites remains in the medium with an abundance of Mg ions and a deficit of Ca ions, and is depressed by methysergide and benanserin. 19 references. (Journal abstract modified)

002791 Kraus, Eric; Le Bars, Daniel; Besson, Jean-Marie. Le Bars: Unite de Recherche de Neurophysiologie Pharmacologique (U. 161), 2 rue d'Alesia, F-75014 Paris, France **Behavioral confirmation of controls" (DNIC) and evidence for a role of endogenous opiates.** Brain Research. 206(2):495-499, 1981.

To evaluate the behavioral significance of diffuse noxious inhibitory controls (DNIC) observed in electrophysiological studies, a behavioral paradigm was designed to determine: 1) whether painful visceral stimulation could mask a complex, centrally integrated response to a punctual noxious stimulus; and 2) whether such inhibition was reduced by moderate doses of naloxone. The vocalization threshold test was used to evaluate hypoalgesic effects of the electric stimulations. Behavioral reactions to the injection of phenylbenzoquinone (PBG) were variable, but a significant increase in vocalization threshold was seen in all Ss. Results show that a dull pain of visceral origin can block the behavioral response to punctual peripheral stimuli. It is contended that this paradigm offers a good experimental model for the phenomenon wherein suffering patients report an increased experimental pain threshold. The hypoalgesia induced by visceral pain is dose dependently antagonized by low dose naloxone, suggesting the involvement of endogenous opiates. 11 references.

002792 Krug, M.; Brodemann, R.; Ott, T. Institute of Pharmacology and Toxicology, Medical Academy, DDR-301 Magdeburg, East Germany **Identical responses of the two hippocampal theta generators to physiological and pharmacological activation.** Brain Research Bulletin. 6(1):5-11, 1981.

Bipolar EEG recordings in the CA1 and dentate gyrus of freely moving rats were examined during conditions of rhythmic slow activity (RSA or theta rhythm) generation by different manipulations. Quantitative EEG parameters of simultaneous records were compared and cross-correlation functions were calculated. Results indicate that even under different conditions of inducing RSA (Physiological activation or injection of arecoline and nicotine) yielding RSA with different frequency characteristics, the quantitative EEG parameters were similar in both recordings. In addition, a high degree of concordance of both EEG recordings was evidenced in the cross-correlation function. These observations are discussed in terms of a high degree of coupling between both RS generators. 21 references. (Author abstract modified)

002793 Krulik, R.; Farska, I.; Jindrova, O. Psychiatric Research Unit, Medical School, Charles University, Ke Karlovu 11, Prague 2, Czechoslovakia **Plasma imipramine levels and demethylase activity in the liver of stressed animals.** Neuropsychobiology. 7(1):12-16, 1981.

The extent to which drug levels and demethylation activity in the rat liver is influenced by stress was investigated. The steady-state values in Ss after a second 14 day period of daily subcutaneous administration of imipramine were the same as during the first period. Liver demethylation activity rose for up to 3 days and then returned to normal. The imipramine binding capacity of the serum brain myelin, synaptosomes and mitochondria did not alter after repeated administration, but a decrease was found in the red blood cells. Stress led to marked reduction of the plasma imipramine level, with a simultaneous increase in liver demethylase activity. Adrenalectomy caused a drop in demethylase activity, while stress had no effect either on these values or on imipramine levels. 8 references. (Author abstract modified)

002794 Kumazawa, T.; Tadaki, E.; Kim, K. Dept. of Physiology, Nagoya University School of Medicine, Showa-ku, Nagoya 466, Japan **Naloxone effects on the blood pressure response induced by thin-fiber muscular afferents.** Brain Research. 205(2):452-456, 1981.

Naloxone effects on the blood pressure level and on the blood pressure responses induced by thin fiber muscular afferent stimulation were studied in anesthetized, bilaterally vagotomized and carotid sinus nerve denervated dogs under artificial ventilation. Repetitive pulses of 8 Hz with various intensities were applied to the gastrocnemius nerve for 1 min while monitoring the compound action potentials. The mean arterial pressure significantly rose about 5 min after a naloxone injection. Compared with the reflexive response in the control period, the depressor effect significantly decreased and the pressor effect significantly increased for 30 min after the injection of naloxone. No correlation was found between naloxone effects on the blood pressure level and on the reflex response, indicating an involvement of different mechanisms with these naloxone effects. It is suggested that endogenous opiates might participate in the regulation of the blood pressure level, as well as of the blood pressure responses caused by thin fiber muscular afferents. 20 references. (Author abstract modified)

002795 Kupersmith, Mark J.; Lieberman, Abraham N. Dept. of Neurology, New York University Medical Center, 550 First Ave., New York, NY 10016 **The effect of specific brain lesions on the high affinity binding of GABA in the substantia nigra.** Brain Research. 194(2):536-539, 1980.

High affinity GABA binding to receptors in the substantia nigra of male Sprague-Dawley rats was studied 21 days after various lesions. Unilateral 6-hydroxydopamine lesions of nigra dopaminergic cells significantly reduced the density of GABA receptors, suggesting GABA receptors are located post synaptically on dopaminergic neurons in the substantia nigra. Electrocoagulation lesions of the globus pallidus did not alter the affinity or density of nigral GABA receptors, but lesions of the crus cerebri induced a two fold increase in the density of nigral GABA receptors. 19 references.

002796 Kuruvilla, Alice; Uretsky, Norman. Divison of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Interaction of chlordiazepoxide and sodium valproate in the nucleus accumbens of the rat.** Life Sciences. 28(4):393-399, 1981.

To determine whether benzodiazepines and sodium valproate interact functionally at GABA receptor sites, graded doses of chlordiazepoxide (CDZ) and sodium valproate were injected bilaterally into the nucleus accumbens and their effect on the dopamine (DA) induced stimulation of motor activity was studied. Both of these compounds, as well as GABA, produced an inhibition of the hyperactivity induced by the bilateral injection of DA into the nucleus accumbens. Bicuculline, the GABA receptor antagonist, blocked the effect of CDZ on the DA induced hyperactivity. A low dose of CDZ, which by itself did not significantly inhibit the effect of DA, potentiated the inhibition of the hyperactivity produced by valproate. These results suggest that CDZ and sodium valproate can interact functionally at GABAergic sites in the CNS. 12 references. (Author abstract modified)

002797 Lai, A. A.; Levy, R. H.; Martis, L. Levy: School of Pharmacy BG 20, University of Washington, Seattle, WA 98195 **Pharmacokinetic profile of valproic acid in rhesus monkeys following single bolus and constant rate intravenous administrations.** Therapie. 35(2):221-232, 1980.

The pharmacokinetic profile of valproic acid was studied. Six male rhesus monkeys received four intravenous bolus doses and later received single step and multistep constant rate intravenous infusion of the drug. Plasma levels were determined by gas liquid chromatography. A one compartment open model with first-order elimination was selected to describe the pharmacokinetics of valproic acid. Results show that the mean parameters from the intravenous bolus studies were: total body clearance, 0.20 liters/hr/kg; elimination half-life, 0.66 hr; and volume of distribution, 0.17 liter/kg. The constant infusion resulted in increases in volume of distribution and half-life. 17 references. (Author abstract modified)

002798 LaManna, Joseph C.; Harik, Sami I.; Light, Andrew I.; Rosenthal, Myron. Dept. of Neurology, University of Miami School of Medicine, Miami, FL 33101 **Norepinephrine depletion alters cerebral oxidative metabolism in the** Brain Research. 204(1):87-101, 1981.

Unilateral chemical lesion of the nucleus locus coeruleus in rats was found to produce unilateral depletion of ipsilateral cortical norepinephrine. Norepinephrine depletion was not associated with changes in resting metabolic balance of the cerebral cortex, as determined by in situ reflection spectrophotometry of the redox state of cytochrome oxidase. Norepinephrine depletion, however, caused slowing of the transient metabolic response to sudden increases in energy demand produced by direct cortical electrical stimulation. The effect was apparent in the redox state of both cytochrome oxidase and nicotinamide adenine dinucleotide, the latter being measured, also in situ, by reflection microfluoremetry. These results demonstrate that norepinephrine has a role in modulating the response to increased metabolic demand in the cerebral cortex. Norepinephrine may mediate its effect by potentiating Na, Kadenosine triphosphatase or through its effects on vascular reactivity. 40 references. (Author abstract modified)

002799 Lambert, J. D. C.; Flatman, J. A. Institute of Physiology, University of Aarhus, DK-8000 Arhus C, Denmark **The interaction between barbiturate anaesthetics and excitatory amino acid responses on cat spinal neurones.** Neuropharmacology. 20(3):227-240, 1981.

Pentobarbitone and thiopentone were injected i.v. or applied iontophoretically during intracellular recording from lumbar motoneurons in anemically decorticated cats. The most striking effect of the barbiturates was a marked reduction in the conductance increase seen during responses to glutamate. Responses to DL-homocysteate were also attenuated by the barbiturates, but no significant interference with conductance changes underlying the response was observed. Results are not consistent with three current theories of the mechanism of action of barbiturate anesthetics, and it is suggested that barbiturates exert their actions through a multitude of mechanisms. 39 references. (Author abstract modified)

002800 Lange, David G.; Roerig, Sandra C.; Fujimoto, James M.; Wang, Richard I. H. Fujimoto: Dept. of Pharmacology and Toxicology, Medical College of Wisconsin, P.O. Box 26509, Milwaukee, WI 53266 **Enhancement of etorphine brain concentrations and changes in etorphine-naloxone pA2 values in morphine-pretreated mice.** Biochemical Pharmacology. 30(2):147-155, 1981.

The enhancement of etorphine brain concentrations and changes in etorphine naloxone pA2 values in morphine pretreated mice were examined. Three hours after pretreatment with morphine, (3H)etorphine was administered subcutaneously, and its brain concentrations were determined as a function of time. Etorphine brain concentrations were higher in morphine pretreated than in saline pretreated animals at 5, 15, 20, and 30 min. This enhancement of brain concentrations was not associated with a change in the analgesic ED50 for etorphine. Morphine pretreatment decreased the etorphine naloxone apparent pA2 value in the direction opposite to that observed for the morphine/naloxone interaction. Results are discussed relative to a morphine induced change in the disposition of etorphine in the brain, or to a morphine induced alteration in morphine, etorphine, and naloxone interactions at agonist and antagonist binding sites. 35 references. (Author abstract modified)

002801 Langer, S. Z.; Dubocovich, M. L. Dept. of Biology Synthelabo (LERS), 58, rue de la Glaciere, F-75013 Paris, France **Cocaine and amphetamine antagonize the decrease of noradrenergic neurotransmission elicited by oxymetazoline but potentiate the inhibition by alpha-methylnorepinephrine in the perfused cat spleen.** Journal of Pharmacology and Experimental Therapeutics. 216(1):162-171, 1981.

Cocaine and amphetamine were found to antagonize the decrease of noradrenergic neurotransmission elicited by oxymetazoline but to potentiate the inhibition by alpha-methylnorepinephrine in the perfused cat spleen. It is noted that the failure of amphetamine to antagonize the inhibition of neurotransmission elicited by the activation of presynaptic dopamine or muscarinic receptors excludes the possibility that the antagonism by amphetamine of the inhibition elicited by oxymetazoline is of a nonspecific nature. Results suggest that differences may exist between the recognition site for catcholamines and for imidazolines at the level of the presynaptic alpha-2 adrenoceptor. It is concluded that the comparison of the order of potencies for imidazolines and phenylethylamines of presynaptic alpha-2 adrenoceptors when neuronal uptake of norepinephrine is inhibited by drugs may need extensive reevaluation. 64 references. (Author abstract modified)

002802 Lau, Christopher; Slotkin, Theodore A. Slotkin: Box 3813, Duke University Medical Center, Durham, NC 27710 **Maturation of sympathetic neurotransmission in the rat heart. VII. Suppression of sympathetic responses by dexamethasone.** Journal of Pharmacology and Experimental Therapeutics. 216(1):6-11, 1981.

The effects of dexamethasone on development of sympathetic nerve function in the heart were evaluated by giving 1mg/kg of dexamethasone s.c. daily for seveal days beginning the day after birth. Dexamethasone interfered with tyramine and isoproterenol induced tachycardia in the neonates but did not cause alterations in development of a marker for presynaptic sympathetic nerve terminals synaptic vesicle uptake of (3H) norepinephrine) nor of postsynatpic beta adrenoceptor binding of (3H)dihydroalprenolol; the deficit was also unrelated to general cellular effects of the hormone. These data suggest that the subnormal chronotropic responses of the heart to sympathetic stimulation in dexamethasone treated neonatal rats result from uncoupling of receptors from the organ response. The effects of dexamethasone on cardiac responses were specific to the neonate, as mature rats given dexamethasone did not show suppression of cardiac sympathetic action. Neonatal dexamethasone treatment also produced a deficit of adrenomedullary development with deficiencies in catecholamine levels and in catecholamine biosynthetic enzymes; deficits in phenylethanolamine N-methyltransferase activity persisted into young adulthood. 36 references. (Author abstract modified)

002803 Leff, Stuart; Adams, Lynne; Hyttel, John; Creese, Ian. Creese: Dept. of Neurosciences, M-008, School of Medicine, University of California, San Diego, La Jolla, CA 92093 **Kainate lesion dissociates striatal dopamine receptor radioligand binding sites.** European Journal of Pharmacology. 70(1):71-75, 1981.

Kainic acid lesions of rat striata reduced the specific dopamine receptor binding of the butyrophenone antagonist 3H-spiperone by 56% and of the butyrophenone like antagonist 3H-domperidone by 59%. High affinity binding of the agonist 3H-N-Propylnorapomorphine (3H-NPA) was reduced by 79% and that of the antagonist 3H-flupenthixol by 73%. Results indicate that 3H-spiperone and 3H-domperidone label dopamine receptors distinct from those labeled by 3H-flupenthixol and 3H-NPA. Data are consistent with the hypothesis that 3H-flupenthixol and 3H-NPA bind preferentially to adenylate linked D1-receptors. 24 references. (Author abstract modified)

002804 Leslie, F. M.; Dunlap, C. E., III; Cox, B. M. Addiction Research Foundation, Palo Alto, CA 94304 **Ascorbate decreases ligand binding to neurotransmitter receptors.** Journal of Neurochemistry. 34(1):219-221, 1980.

The effect of ascorbate on ligand binding to several neurotransmitter receptors in guinea-pig brain was examined. Opiate and clonidine binding sites were sensitive particularly to the destructive effects of ascorbate, but the densities of haloperidol and quinuclidinyl benzilate binding sites were reduced also. The receptor destruction induced by ascorbate was inhibited by ethylene-diaminetetraacetate, suggesting the involvement of ascorbate catalyzed lipid peroxidation. Results provide no evidence that neurotransmitter receptors are subject to ascorbate catalyzed destruction under physiological conditions, but the findings do indicate that ligand binding properties of neurotransmitter receptors are modified by exposure to ascorbate at concentrations frequently used in ligand binding studies. 15 references.

002805 Lewis, Darrell V., Jr. Division of Pediatric Neurology, Duke University Medical Center, Box 3533, Durham, NC 27710 **Diphenylhydantoin reduces the outward current of the action potential in Aplysia.** Brain Research. 207(1):234-238, 1981.

Diphenylhydantoin (DPH) has been shown to prolong the repolarization phase of action potentials in aplysia and to reduce the spike after hyperpolarization. Somata of aplysia giant neurons were voltage clamped and action potential currents were measured to determine what alterations might be responsible for the prolonged repolarization and reduced undershoot. DPH did not affect the peak inward current; however, it did reversibly reduce the outward current at concentrations of 38mcM or greater. The data indicate that DPH reduced the voltage sensitive potassium conductance rather than the A-current or the calcium activated potassium conductance. These changes in outward current would explain the prolonged action potentials and reduced after hypopolarization seen with DPH in aplysia. 14 references. (Author abstract modified)

002806 Lin, M. T.; Chandra, A.; Ko, W. C.; Chen, Y. M. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan **Serotonergic mechanisms of clonidine-induced hypothermia in rats.** Neuropharmacology. 20(1):15-21, 1981.

The effects of intraventricular administration of clonidine and serotonin on metabolic, respiratory, and vasomotor activities as well as on body temperature were assessed in unanesthetized rats at ambient temperatures of 8, 22, and 30 degrees C. Intraventricular administration of clonidine and serotonin each produced a dose dependent hypothermia at all temperatures studied. At 8 degrees and 22 degrees C, the hypothermia in response to clonidine and serotonin was due to decreased metabolic heat production, increased respiratory evaporative heat loss and cutaneous vasodilation. In the heat, the induced hypothermia was due to increased respiratory evaporative heat loss. The clonidine hypothermia was greatly antagonized by the pretreatment of animals with 5,7-dihydroxytryptamine, but not with 6-hydroxydopamine. The data indicate that clonodine may decrease heat production and (or) increase heat loss to elicit hypothermia, probably via activation of central serotonergic pathways. 24 references. (Author abstract modified)

002807 Lindvall, M.; Owman, C. Dept. of Histology, University of Lund, Biskopsgatan 5, S-223 62 Lund, Sweden **Evidence for the presence of two types of monoamine oxidase in rabbit choroid plexus and their role in breakdown of amines influencing cerebrospinal fluid formation.** Journal of Neurochemistry. 34(3):518-522, 1980.

The presence of monoamine oxidase (MAO) in the choroid plexus of rabbit brain ventricles was demonstrated radiometrically. Histochemical staining of MAO indicated the enzyme was located primarily in the secretory epithelium. Inhibition by clorgyline and deprenyl showed that type-A and type-B MAO were present in approximately equal proportions in the plexus. Intraventricular administration of nialamide markedly reduced cerebrospinal fluid (CSF) production and potentiated the reduction in CSF formation induced by intraventricular adminstration of noradrenaline. The nialamide effect was diminished after sympathetic denervation of the plexus, indicating that neuronal MAO is also present in the plexus. 20 references. (Author abstract modified)

002808 Lodge, D. Dept. of Pharmacology, Australian National University, Canberra, Australia **L-Histidine: effects on sensitivity of cat spinal neurones to amino acids.** Neuroscience Letters. 14:171-176, 1979.

Evidence is presented that L-histidine enhances the inhibitory actions of GABA, muscimol, and beta-alanine rather than that of glycine on spinal neurons in pentobarbitone anesthetized cats. L-histidine also enhanced the excitatory action of L-glutamate, D-aspartate, L-aspartate, L-homocysteate, and especially that of quisqualate. The actions of acetylcholine, kainate, N-methyl-D-aspartate, and D-homocysteate were more commonly reduced. These actions of L-histidine are best described to an effect on amino acid transport systems, probably of the low affinity type, which therefore appear to be partially responsible for the inactivation of exogenously administered amino acids. (Journal abstract)

002809 Loew, D. M. Preclinical Research, Pharmaceutical Division, Sandoz Ltd., Basel, Switzerland **Pharmacologic approaches to the treatment of senile dementia.** In: Amaducci, L., Aging of the brain and dementia, vol. 13. New York, Raven, 1980. 326 p. (p. 287-294).

Pharmacological approaches to the treatment of senile dementia are examined, along with animal effects of three representative drugs (vincamine, piracetam, and co-dergocrine mesylate), and trends in gerontopsychopharmacological research. A review of the animal studies with the three drugs indicates that the pharmacological basis for their therapeutic effects involves influences on cerebral blood flow, brain cell metabolism, and synaptic transmission. Present research in animals and humans is moving away from investigations of vascular mechanisms and emphasizes drugs that interact with brain neurotransmission to mitigate the cognitive and emotional symptoms of senile mental deterioration. 63 references. (Author abstract modified)

002810 Login, Ivan S.; MacLeod, Robert M. Dept. of Neurology, University of Virginia School of Medicine, Charlottesville, VA 22908 **The direct effect of reserpine in vitro on prolactin release from rat anterior pituitary glands.** Brain Research. 204(1):79-85, 1981.

The direct effect of reserpine in vitro on prolactin release from rat anterior pituitary glands was investigated. Anterior pituitary glands from normal untreated rats synthesize and release the hormone prolactin (Prl) during incubation under in vitro conditions. Addition of dopamine (DA) greatly inhibits the release of Prl and to a lesser extent reduces Prl synthesis. When pituitary glands are incubated in the presence of reserpine, there is a similar significant dose related inhibition of Prl release. This effect persists even in the presence of a DA antagonist (haloperidol) and after the depletion of hypothalamic amines by in vivo treatment with reserpine. Reserpine in vitro also inhibits release of newly synthesized growth hormone from the pituitary glands of male rats; however, this is not observed when female rats are studied. It is concluded that the direct effect of reserpine to inhibit Prl release is apparently independent of any interaction with catecholamine systems and is mediated by other, presently undefined mechanisms. 19 references. (Author abstract modified)

002811 Longshore, Margaret A.; Makman, Maynard H. Dept. of Biochemistry, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461 **Stimulation of retinal adenylate cyclase by vasoactive intestinal peptide (VIP).** European Journal of Pharmacology. 70(2):237-240, 1981.

The effects of vasoactive intestinal peptide (VIP), secretin, and glucagon on retinal adenylate cyclase were studied in rabbit, rat, and calf retinas. Results revealed the presence of a highly active VIP sensitive adenylate cyclase in mammalian retina. The peptide effects were not enhanced by the guanine nucleotide analog 5'-guanylyl-imidodiphosphate. Glucagon and secretin also caused significant increases in retinal adenylate cyclase activity, but the magnitude of these effects was generally less that that of VIP. 10 references. (Author abstract modified)

002812 Lorez, Hanspeter. Pharma Research Dept., F. Hoffmann-La Roche and Co., Ltd., CH-4002 Basle, Switzerland **Fluorescence histochemistry indicates damage of striatal dopamine nerve terminals in rats after multiple doses of methamphetamine.** Life Sciences. 28(8):911-916, 1981.

The effects of methamphetamine on fluorescence histochemistry of dopamine nerve fibers in neostriatum, nucleus accumbens, tuberculum olfactorium and medial frontal cortex were investigated in rats treated every 6 hours for 24 hours and killed 6 and 11 days after treatment. In control rats, occasional nerve fibers (probably nerve terminals) in the neostriatum showed some distortion and a strong formaldehyde-glyoxylic acid induced catecholamine fluorescence; 6 and 11 days after methamphetamine, the number of swollen nerve fibers showing strong fluorescence in this region was significantly increased. In contrast, in nucleus accumbens, tuberculum olfactorium, and medial frontal cortex, such fiber swellings were virtually absent in both controls and methamphetamine treated rats. These findings indicate that multiple doses of methamphetamine might be toxic to neostriatal dopamine nerve fibers. 22 references. (Author abstract modified)

002813 Lyness, William H.; Mycek, Mary J. College of Medicine and Dentistry of New Jersey, New Jersey Medical School, Dept. of Pharmacology, 100 Bergen St., Newark, NJ 07103 **In vitro cellular adaptation of serotonergic processes after chronic central phenobarbital administration.** Brain Research. 204(1):248-252, 1981.

An attenuation of phenobarbital induced depression of potassium (K) stimulated (3H)serotonin (5-HT) release in brain slices from rats made tolerant to icv injected phenobarbital is reported. Uptake of (3H)5-HT was not influenced either by the tolerant state of the animal or by the presence of phenobarbital in the incubation medium. Although stimulation of (3H)5-HT release after K induced depolarization varied with the tissue, tolerance had no effect on the magnitude of this effect. Addition of phenobarbital to the medium reduced K stimulated amine release in a dose dependent manner. Tolerance was found to play a role in determining the extent to which exogenous phenobarbital depressed 5-HT release; in these instances, a parallel shift to the right of the dose response curve was observed. 14 references.

002814 Makman, Maynard H.; Dvorkin, B.; Horowitz, Sara G.; Thal, Leon J. Dept. of Biochemistry, Albert Einstein College of Medicine, Bronx, NY **Properties of dopamine agonist and antagonist binding sites in mammalian retina.** Brain Research. 194(2):403-418, 1980.

Stereospecific binding sites for the dopamine antagonist 3H-spiroperidol were found in retinal homogenates of calf, rat, rabbit, and Cebus appella and Macaca mulata monkeys. In additional studies of calf and rat retina, stereospecific binding sites were found for the dopamine agonist 3H-2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronapththalene (3H-ADTN). The total number of 3H-ADTN sites in retina was at least twice that of 3H-spiroperidol sites. Guanine nucleotides reduced the affinity of ADTN for 3H-spiroperidol binding and also reduced the specific binding of 3H-ADTN itself. It is suggested that 3H-ADTN sites sensitive to guanine nucleotides may be related to guanine nucleotide sensitive 3H-spiroperidol sites as well as to adenylate cyclase. The 3H-ADTN sites that are not sensitive to guanine nucleotides may be presynaptic and are probably not coupled to adenylate cyclase. 28 references. (Author abstract modified)

002815 Marshall, John F. Department of Psychobiology, University of California, Irvine, CA 92717 **Basal ganglia dopaminergic control of sensorimotor functions related to motivated behavior.** In: Thompson, R., Neural mechanisms of goal-directed behavior & learning. New York, Academic Press, 1980. 639 p. (p. 167-176).

Research data, which indicate that dopamine (DA) containing neurons of the rat brain are critical to certain sensorimotor capacities, most notably to its ability to orient toward tactile, visual, and olfactory stimuli, are reviewed. The sensorimotor deficits of rats with damage to these neurons appears to contribute to the initial aphagia and may contribute as well to the later stages of the syndrome of ingestive deficits. The remarkable capacity of these rats to recover from sensorimotor deficits appears related to compensatory neurochemical events occurring at remaining dopaminergic synapses. First, administration of a DA receptor stimulant to animals with severe DA depletions can restore orientation capacities, suggesting that a restitution of DA receptor activity is sufficient for behavioral recovery to occur. Second, administration of drugs that interfere with DA neurotransmission to animals that have spontaneously recovered from their somatosensory inattention reinstates sensorimotor dysfunction, suggesting that a restitution of DA receptor activation may be necessary for behavioral recovery. 23 references.

002816 Martinet, Michel; Fonlupt, Pierre; Pacheco, Henri. Institut National des Sciences Appliquees, Service de Chimie Biologique, Bat. 406, 20 Avenue Einstein, F-69621 Villeurbanne cedex, France **Activation of soluble striatal tyrosine hydroxylase in the rat brain after CDPcholine administration.** Biochemical Pharmacology. 30(5):539-541, 1981.

The in vivo and in vitro effects of the antiparkinsonian drug, cytidine 5'diphosphorylcholine (CDPcholine), on the activity of tyrosine hydroxylase, the rate limiting enzyme in the synthesis of catecholamines, in rat brain were investigated. CDPcholine was unable to modify tyrosine hydroxylase activity when added in vitro at different concentrations. A single injection of CDPcholine in vivo caused striatal tyrosine hydroxylase activity to increase by 12%, 24%, and 25% after 30, 60, and 120 minutes. The high DMPH4 level used could suppress CDPcholine alteration induced in vitro; however, this does not occur after CDPcholine administration with the same DMPH4 level. Thus, the hypothesized in vitro activation by CDPcholine seems doubtful. Two types of action of CDPcholine are proposed: 1) disinhibition of striatal tyrosine hydroxylase due to increased release and inhibited reuptake of dopamine; and 2) activation of striatal tyrosine hydroxylase by inducing an active physical form. The pharmacological impact could be participation in lipid metabolism. 13 references.

002817 Marton, J.; Molnar, J.; Koves, K.; Halasz, B. Second Dept. of Anatomy, Semmelweis University Medical School, P.O.B. 95, H-1094 Budapest, Hungary **Naloxone reversal of the pentobarbital induced blockade of ovulation in the rat.** Life Sciences. 28(7):737-743, 1981.

The effect of naloxone, an opiate antagonist, on the pentobarbital induced suppression of gonadotrophin secretion and subsequent ovulation was studied. Two injections of naloxone, the first at 13:00 hours and the second, given simultaneously with an ovulatory blocking dose of pentobarbital at 13:30 hours, partially reversed the inhibitory effect of the barbiturate. However, if the first injection of naloxone was given with pentobarbital at 13:30 hours and a second at 14:30 hours, then the opioid antagonist had no such effect. Naloxone administered alone enhanced gonadotrophin secretion and increased the number of ova shed. These findings support the view that endogenous opioids may exert an inhibitory influence on central neural processes involved with ovulation. 27 references. (Author abstract modified)

002818 Mayer, M. L. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **A barbiturate evoked intensification of postsynaptic inhibition in the preoptic ovulatory trigger region of the hypothalamus.** Brain Research. 207(1):229-233, 1981.

A barbiturate evoked intensification of postsynaptic inhibition in the preoptic ovulatory trigger region of the hypothalamus is described. Extracellular single unit recordings were used to study inhibitory synaptic responses evoked from preoptic/anterior hypothalamic neurons following arcuate/ventromedial stimulation. Intravenously administered methohexitone, pentobarbitone and thiopentone increased the duration of inhibitory synaptic responses by up to 400%. Submaximal response to iontophoretically applied GABA but no glycine were also potentiated. Recovery from the actions of the short acting barbiturates was observed. 20 references. (Author abstract modified)

002819 Mazzari, S.; Massotti, M.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **GABA receptors as supramolecular units.** Advances in Biochemical Psychopharmacology. 26:1-8, 1981.

A model of the GABA receptor as a supramolecular unit is presented, and procedures whereby the GABA recognition protein and GABA-modulin can be isolated, stabilized, and purified are discussed. Preliminary recombination experiments show that the GABA-modulin inhibits the binding of GABA to the fluidified GABA recognition sites. Since the fluidified GABA recognition site does not bind benzodiazepines and since benzodiazepines added to the fluidified GABA recognition protein fail to modify the binding of GABA, it is suggested that the benzodiazepine binding protein is not the protein that recognizes GABA. Since activation of the benzodiazepine recognition protein modifies GABA receptor function and since this differs from the protein which contains the GABA recognition site, it can be inferred that the GABA receptor includes at least four proteins: GABA-modulin, the protein that contains the GABA recognition site, the protein that contains benzodiazepine recognition sites, and the Cl- ion channel. 18 references. (Author abstract modified)

002820 McCarthy, Ken D.; Harden, T. Kendall. Harden: Dept. of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Identification of two benzodiazepine binding sites on cells cultured from rat cerebral cortex.** Journal of Pharmacology and Experimental Therapeutics. 216(1):183-191, 1981.

THe identification of two benzodiazepine binding sites on cells cultured from rat cerebral cortex is described. Cultures containing either glia alone, predominately neurons alone or neurons and glia were prepared from perinatal rat cerebral cortex. Cells in these cultures exhibited both a high and a low affinity binding site for (3H)flunitrazepam. The pharmacological properties of this low affinity binding site were markedly different from the binding site present on neurons but similar to those of a binding site on C6 rat glioma cells. The high affinity binding site appeared to be restricted to neuronal elements in these cultures. 31 references. (Author abstract modified)

002821 McConnell, Susan K.; Baum, Michael J.; Badger, Thomas M. Baum: Massachusetts Institute of Technology, 37-331, Cambridge, MA 02139 **Lack of correlation between naloxone-induced changes in sexual behavior and serum LH in male rats.** Hormones and Behavior. 15(1):16-35, 1981.

Four experiments were conducted to determine whether the action of opiate receptor antagonist drugs on sexual performance in male rats is mediated by the central release of luteinizing hormone releasing hormone (LHRH). In Experiment 1 it was demonstrated that the administration of naloxone caused a lengthening of postejaculatory intervals and an elevation of serum luteinizing hormone (LH) concentrations in gonadally intact male rats. In Experiment 2 manipulation of females' proceptive and receptive behaviors failed to reveal the reductions in ejaculation latencies and reductions in the number of intromissions preceding ejaculation which have been reported previously, after administration of naloxone to male rats. In Experiment 3 pinching the tails every 30 sec after ejaculation partially abolished the relative refractory periods of the postejaculatory intervals. In Experiment 4 naloxone was given to castrated males implanted with testosterone filled silastic capsules which produced a wide range of basal serum LH concentrations. Naloxone caused an increase in postejaculatory intervals. However, this effect was not correlated with the degree to which naloxone stimulated serum LH, suggesting that the effects of naloxone on the postejaculatory interval are not mediated by a drug induced release of LHRH. 35 references. (Author abstract modified)

002822 McDougal, J. N.; Marques, P. R.; Burks, T. F. Dept. of Pharmacology, Arizona Health Sciences Center, Tucson, AZ 85724 **Reduced tolerance to morphine thermoregulatory effects in senescent rats.** Life Sciences. 28(2):137-145, 1981.

Age related differences in thermoregulatory responses to acute or chronic morphine administration were investigated. Precipitated withdrawal was also analyzed by inducing withdrawal with naloxone in morphine pellet implanted rats. Senescent (26-month-old or 27-month-old), mature (10-month-old or 11-month-old), and young (3-month-old or 4-month-old) male

Fischer 344 rats were restrained and changes in rectal temperature were monitored for six hours after morphine administration. Results indicate that older rats are more resistant to the acquisition of tolerance to the thermic effect of morphine; however, with continued morphine treatment, rats become tolerant, regardless of age. 21 references. (Author abstract modified)

002823 McGaugh, James L.; Martinez, Joe L., Jr.; Jensen, Robert A.; Messing, Rita B.; Vasquez, Beatriz, J. Department of Psychobiology, University of California, Irvine, CA 92717 **Central and peripheral catecholamine function in learning and memory processes.** In: Thompson, R., Neural mechanisms of goal-directed behavior & learning. New York, Academic Press, 1980. 639 p. (p. 75-91).

Research data on animals are presented to show that retention of newly learned responses is influenced by peptide hormones, catecholamines, and drugs that affect hormone and catecholamine metabolism. These findings provide support for the view that processes associated with affective states modulate memory storage. The role of peripheral hormonal systems in the modulation of memory storage is emphasized. The finding that memory is influenced by experimentally induced alterations in peripheral hormonal systems emphasizes the possibility that learning normally involves the release of peripheral hormones that then influence brain processes involved in memory storage. Such a view does not assume that learning requires such feedback. Rather, it seems that the feedback does occur and that involvement of peripheral hormonal systems may be important for regulating the degree or strength of retention of recent experiences. Viewed in this way, the importance of an experience may be defined by its consequences for peripheral hormonal systems. 27 references.

002824 McGeer, P. L.; McGeer, E. G.; Innanen, V. T. Kinsmen Lab. of Neurological Research, Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Kainic acid and neurotransmitter interactions in the basal ganglia.** Advances in Biochemical Psychopharmacology. 24:185-191, 1980.

Studies of kainic acid (KA) and neurotransmitter interactions in the rat basal ganglia are described. It is noted that KA is a unique tool for neuroscientists, and has been used widely to resolve disputes as to which type of structure is involved in various neurochemical or behavioral effects of electrolytic lesions and in localizing various biochemical markers to specific types of structures within the lesion area. Studies of KA and 6-hydroxydopamine, a selective toxin for dopaminergic neurons have demonstrated the apparent presence of heterologous neurotransmitter receptor sites on nerve endings and thus indicated the possibility of dendro/axonic transmission in the nervous system. It is noted if dendro/axonic transmission is a general phenomenon in CNS, then there are important implications for development of neuroleptics and other pharmacological agents for clinical use. 27 references.

002825 McSwigan, John D.; Nicol, Susan E.; Gottesman, I. I.; Tuason, V. B.; Frey, William H., II. Frey: Dept. of Psychiatry, Research Unit, St. Paul-Ramsey Medical Center, St. Paul, MN 55101 **Effect of dopamine on activation of rat striatal adenylate cyclase by free Mg2 and guanyl nucleotides.** Journal of Neurochemistry. 34(3):594-601, 1980.

Stimulation of male Sprague-Dawley rat striatal adenylate cyclase by guanyl nucleotides was examined, using magnesium adenosine triphosphate or magnesium 5'-adenylylimidodiphosphate as substrate. Guanosine triphosphate (GTP) and 5'-guanylylimidodiphosphate stimulated adenylate cyclase under conditions in which the guanyl nucleotide was not degraded. The apparent stimulation of adenylate cyclase by guanosine diphosphate (GDP) was due to an ATP dependent transphosphorylase in the tissue that converts GDP to GTP. These findings indicate that GTP is the physiological guanyl nucleotide responsible for stimulation of striatal adenylate cyclase. Dopamine appeared to stimulate striatal adenylate cyclase by increasing the affinity for free magnesium ion and guanyl nucleotide and by increasing maximal velocity. The effect of dopamine was blocked by the antipsychotic drug fluphenazine. 45 references. (Author abstract modified)

002826 Meldrum, Brian. Dept. of Neurology, Institute of Psychiatry, London SE5 8AF, England **GABA-agonists as anti-epileptic agents.** Advances in Biochemical Psychopharmacology. 26:207-217, 1981.

Studies of the anticonvulsant action of GABA agonists are reviewed, and the paradoxical epileptogenic action of classical GABA agonists (i.e., those acting on postsynaptic inhibition that is bicuculline sensitive and strychnine insensitive) is discussed. The issue of whether this effect is due to action on other GABA receptors or is a consequence of diffuse action on classical GABA receptor sites is evaluated. Results indicate that GABA agonists appear to be anticonvulsant in some rodent test systems, but are epileptogenic rather than anticonvulsant in a primate model of epilepsy. 33 references.

002827 Meldrum, M. J.; Isom, G. E. Dept. of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Role of monoaminergic systems in morphine-induced respiratory depression.** Neuropharmacology. 20(2):169-175, 1981.

Morphine sulfate (80mg/kg) induced respiratory depression in Sprague-Dawley rats was accompanied by an increase in 5-hydroxytryptamine (5-HT) and a decrease in norepinephrine (NE) in the medulla/pons area. The morphine induced respiratory depression was potentiated by pretreatment with drugs that increase 5-HT levels and was antagonized by pretreatments that increase NE levels. It is suggested that 5-HT functions as a depressant mediator and NE as an excitatory mediator in morphine induced respiratory depression. Naloxone appears to reverse the respiratory depression by altering the serotonergic component of the action of morphine. 34 references. (Author abstract modified)

002828 Memo, M.; Riccardi, F.; Trabucchi, M.; Spano, P. F. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Localization of GABA and dopamine receptor sites in retinal glial cells using DL-alpha-aminoadipic acid.** Advances in Biochemical Psychopharmacology. 26:41-51, 1981.

Studies of the localization of GABA and dopamine receptor sites in retinal glial cells using DL-alpha-aminoadipic acid (AA) are described. Topics discussed include the: gliotoxic action of AA; action of AA on marker enzymes for neurons and glial cells; action of AA on GABA receptor binding; action of AA on dopamine receptor binding; and the action of kainic acid on GABA and dopamine receptor binding. Results agree with the interpretation that the action of AA ultimately elicits a denaturation of GABA and dopamine receptor proteins present on the membrane of retinal glial cells. It is suggested that a substantial portion of dopamine receptors in the retina are not functionally linked to adenylyl cyclase activity (D2-type). 29 references.

002829 Minneman, Kenneth P.; Pittman, Randall N.; Molinoff, Perry B. Dept. of Pharmacology, University of Colorado Health Sciences Center, Denver, CO 80262 **Beta-adrenergic receptor subtypes: properties, distribution, and regulation.** Annual Review of Neuroscience. 4:419-461, 1981.

The properties, cellular localization, and regulation of beta-adrenergic receptor sybtypes are reviewed. Data obtained in studies with intact animals and isolated organs and with radioligand binding assays are considered. Changes in cortical and cerebellar beta-adrenergic receptors during development and aging are described. 182 references.

002830 Mon, Manuel J.; Haas, Ali E.; Stein, Janet L.; Stein, Gary S. G. Stein: Dept. of Biochemistry and Molecular Biology, University of Florida College of Medicine, Gainesville, FL 32610 **Influence of psychoactive and nonpsychoactive cannabinoids on cell proliferation and macromolecular biosynthesis in human cells.** Biochemical Pharmacology. 30(1):31-43, 1981.

The influennce of psychoactive cannabinoids delta9-tetrahydrocannabinol (delta9-THC), delta8-THC, and 11-OH-delta9-THC) and nonpsychoactive cannabinoids (cannabinol) on proliferation of human cells (HeLa S3 cells grown in suspension culture) and on biochemical events associated with the proliferative process were examined. The four cannabinoids studied brought about a dose dependent inhibition in cell growth. Pulse labeling studies indicate a cannabinoid induced decrease in incorporation of (3H)thymidine, (3H)uridine, and (3H)leucine into DNA, RNA, and protein, respectively, in intact cells; in most cases, a comparable decrease in the acid soluble intracellular precursor pools was observed. Results from in vitro nuclear and chromatin transcription experiments do not suggest a drug induced change in RNA synthesis. It appears, therefore, that quantitative alterations in the synthesis and/or turnover of nucleic acids and proteins do not result from cannabinoid treatment of HeLa cells. 48 references. (Author abstract modified)

002831 Mon, Manuel J.; Haas, Ali E.; Stein, Janet L.; Stein, Gary S. G. Stein: Dept. of Biochemistry and Molecular Biology, University of Florida College of Medicine, Gainesville, FL 32610 **Influence of psychoactive and nonpsychoactive cannabinoids on chromatin structure and function in human cells.** Biochemical Pharmacology. 30(1):45-58, 1981.

The influences of two naturally occurring psychoactive cannabinoids (delta9-tetrahydrocannabinol (THC) and delta8-THC), of a psychoactive cannabinoid metabolite (11-OH-delta9-THC), and of a nonpsychoactive cannabinoid (cannabinol) on the composition, metabolism, and structure of human (HeLa cell) chromatin were examined. The effects of all four cannabinoids on the composition and synthesis of chromosomal proteins were studied by pulse labeling with (3H)leucine. The relative amounts of both histones and nonhistone chromosomal proteins remained unaffected, but a decrease in (3H)leucine incorporation into both histones and nonhistone proteins was observed. Posttranslational acetylation and phosphorylation of chromosomal proteins were studied in cannabinoid treated cells by pulse labeling with (3H)acetate and (32P). Variations were observed in (3H)acetate incorporation into histones and (32P) incorporation into both histones and nonhistone chromosomal proteins. Pancreatic DNase I digestion of chromatin from cannabinoid treated HeLa cells failed to demonstrate any drug induced alteration in DNA/protein interactions. 54 references. (Author abstract)

002832 Mos, Jan; Broxterman, Henk J.; Van Bennekom, Wouter P. Dept. of Pharmacology, Sylvius Laboratories, Wassenaarseweg 72, NL-2333 AL Leiden, The Netherlands **In vivo voltammetric investigations into the action of HA-966 on central dopaminergic neurons.** Brain Research. 207(2):465-470, 1981.

In vivo voltammetric investigations of the action of HA-966, an agent known to depress the firing rate of central dopaminergic nerve cells, on central dopaminergic neurons are described. Simultaneously, levels of the drug itself were detected in the striatum. Injection of HA-966 resulted in a decrease in the oxidation current Iox at 0.3V and the appearance of a new oxidation peak at about 0.9V. The decrease in Iox can be ascribed to a decrease of the extracellular dopamine (DA) concentration, owing to a blockade of overall DA release. Since HA-966 does not affect 5-hydroxytryptamine (5-HT) levels nor noradrenaline (NA) levels in the striatum, it is unlikely that changes in the release of these transmitters should be involved in the decrease of Iox. Results indicate that some HA-966 is transported into the brain. 16 references. (Author abstract modified)

002833 Muller, Walter E. Pharmakologisches Institut, Universitat Mainz, Obere Zahlbacher Strasse 67, D-6500 Mainz, West Germany **The benzodiazepine receptor: an update.** Pharmacology. 22(3):153-161, 1981.

Recent research on the brain specific binding sites of benzodiazepines is reviewed. Biochemical and pharmacological data indicate that benzodiazepine receptors are the endogenous targets that mediate the pharmacological effects of benzodiazepines. Considerable evidence indicates that the benzodiazepine receptor serves as an amplifying system for GABA mediated transmission by increasing the affinity of the GABA receptor. The endogenous ligand of the benzodiazepine receptor has not yet been identified. 63 references. (Author abstract modified)

002834 Muraki, T.; Tokunaga, Y.; Nakadate, T.; Kato, R. Dept. of Pharmacology, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan **Increase in plasma cyclic AMP levels elicted by naloxone in morphine-dependent male mice.** Neuropharmacology. 20(2):177-181, 1981.

Naloxone increased the levels of plasma cyclic AMP in morphine dependent male ddY mice, but not in controls. The effect of naloxone was inhibited by pretreatment with propranolol, hexamethonium, or adrenalectomy, but not by atropine or phentolamine. Results suggest that naloxone increases the level of plasma cyclic AMP by releasing catecholamines from the adrenal medulla, thereby activating adenylate cyclase in the tissues through stimulation of beta-adrenergic receptors. It is suggested that the increase in plasma cyclic AMP may be used as an index of the severity of withdrawal symptoms and degree of physical dependence in laboratory animals treated with morphine like drugs. 15 references. (Author abstract modified)

002835 Murphy, Kenneth M. M.; Snyder, Solomon H. Dept. of Neuroscience, Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Adenosine receptors in rat testes: labeling with 3H-cyclohexyladenosine.** Life Sciences. 28(8):917-920, 1981.

Adenosine receptors in rat tissues were labelled with 3H-N6-cyclohexyladenosine (3H-CHA) and the distribution and drug specificity of these binding sites throughout the body were evaluated. Detectable receptor concentrations are restricted to the brain and testes. The brain displays receptor levels of 9 pmoles/g wet weight of tissue while the testes display 2 pmoles/g, with all other tissues examined showing less than detectable specific binding of 3H-CHA. The receptors in these two tissues appear to possess identical pharmacologic profiles with an A1 specificity for both. No change in the total number of 3H-CHA binding sites is seen in testes of rats which had been hypophysectomized 14 days prior to sacrifice. This may exclude the Leydig cells as a source of adenosine receptors in the rat testes. 12 references. (Author abstract modified)

002836 Nadi, N. S.; Hirsch, J. D.; Margolis, F. L. Margolis: Roche Institute of Molecular Biology, Dept. of Physiological Chemistry and Pharmacology, Nutley, NJ 07110 **Laminar distribution of putative neurotransmitter amino acids and ligand bind-**

ing sites in the dog olfactory bulb. Journal of Neurochemistry. 34(1):138-146, 1980.

The laminar distribution of 10 amino acids, the dipeptide carnosine, and 9 (3H)ligand binding sites in four anatomically distinct layers of coronal sections of frozen dog olfactory bulb were determined. GABA and tyrosine levels were highest in the mitral cell/granule cell layer, and glutamate levels were slightly elevated in the glomerular layer. The distributions of other amino acids did not show significant differences across layers. Muscimol, diazepam, kainic acid, and spiroperidol binding were predominantly localized in the mitral cell/granule cell layer, where clonidine binding was at a minimum. Dihydromorphine binding was high in both the fiber and mitral cell/granule cell layers. Carnosine binding was maximal in the glomerular layer. 44 references. (Author abstract modified)

002837 Nakahama, Hiroshi; Shima, Keisetsu; Aya, Kojiro; Kisara, Kensuke; Sakurada, Shinobu. Div. of Neurophysiology, Institute of Brain Diseases, Tohoku University School of Medicine, 1-1 Seiryo-Cho, Sendai, Japan **Antinociceptive action of morphine and pentazocine on unit activity in the nucleus centralis lateralis, nucleus ventralis lateralis and nearby structures of the cat.** Pain. 10(1):47-56, 1981.

Single neuronal activity was recorded extracellularly from the nucleus centralis lateralis (CL), ventralis lateralis (VL), and medialis dorsalis (MD) of the cat thalamus. The majority of the CL, VL, and MD neurons were excited by nociceptive stimulation such as pinching the skin with serrated forceps and/or intraarterial injection of bradykinin. The nociceptive neurons were driven also by nonnociceptive stimulation such as tap of deep tissues, bending hairs with an air puff and/or joint rotation, and their receptive fields were large. After intravenous administration of either morphine or pentazocine, most nociceptive neurons became unresponsive to nociceptive stimuli, although they were driven by nonnociceptive stimuli. It is suggested that morphine and pentazocine have a specific antinociceptive action on these nociceptive neurons. Intravenous naloxone reversed the antinociceptive action of morphine, but failed to reduce the action of pentazocine. It is maintained that this differentiation has an important functional significance. 38 references. (Author abstract)

002838 Nathanson, James A.; Redmond, D. Eugene, Jr. Dept. of Neurology, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114 **Morphine withdrawal causes subsensitivity of adrenergic receptor response.** Life Sciences. 28(12):1353-1360, 1981.

To determine whether the hyperactivity of noradrenergic neurons that occurs during opiate withdrawal might be associated with a reciprocal alteration in noradrenergic receptor response, isoproterenol stimulated adenylate cyclase activity was examined in the cerebella of morphine addicted monkeys at two time periods: 1) prior to withdrawal; and 2) during late withdrawal. Compared to control Ss, the chronically addicted group showed a significant increase in maximal enzyme velocity, a finding consistent with the observed hypoactivity of noradrenergic neurons which occurs during opiate administration. In contrast, the morphine withdrawal group demonstrated a significant decrease in enzyme activity. Piperoxan, known to mimic the effects of withdrawal in causing noradrenergic hyperactivity, also decreased enzyme activity. In no group was there a change in Ka for isoproterenol. These findings, indicating that opiate withdrawal is associated with a subsensitivity of noradrenergic receptor response, suggest a possible etiology for certain of the physiological changes of noradrenergic hypoactivity seen during the secondary (or protracted) abstinence syndrome. 44 references. (Author abstract)

002839 Neethling, Andries C.; McCarthy, Brian W.; Taljaard, Joshua J. F. MRC Neurochemistry Research Group, Dept. of Chemical Pathology, University of Stellenbosch, P. O. Box 63, Tygerberg 7505, South Africa **Characterization and quantitation of alpha-adrenergic receptor subtypes in rat hypothalamus.** Biochemical Pharmacology. 30(6):565-569, 1981.

The binding of (3H)dihydroergocryptine ((3H)DHE) to rat hypothalmic membranes was examined. Displacement of (3H)DHE by 100nM phentolamine, prazosine, and clonidine was used to assay for total alpha-adrenergic, alpha-1 adrenergic, and alpha-2 adrenergic receptor sites respectively. The alpha-1 adrenergic receptor content of the hypothalmus is 4.1pmoles/g tissue whereas the alpha-2 level is 6.5pmoles/g tissue. (3H)WB 4101 (alpha-1 selective) and (3H)clonidine (alpha-2 selective) binding yielded similar levels of 3.2 and 5.8pmoles/g tissue. It is concluded that (3H)DHE is a suitable ligand for the assay of alpha-adrenergic receptor subtypes under the conditions determined in this study. 20 references. (Author abstract)

002840 Nestoros, Joannis N. McGill University (Canada) **Antianxiety agents and synaptic transmission in the brain: electrophysiological studies. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):2916-B, 1981. (Not available from Univ. Microfilms), 1980.

The effects of antianxiety agents on the inhibitory effects of iontophoretically applied GABA and electrically evoked inhibition in the cerebral cortex of the cat were examined. Flurazepam and ethanol potentiated the inhibitory effects. The degree of potentiation produced by five benzodiazepines correlated with their relative affinities for the benzodiazepine receptor when all five drugs were applied with equal iontophoretic doses, and was not significantly different from one drug to another when the benzodiazepines were applied in doses inversely proportional to their relative affinities for the benzodiazepine receptor. Iontophoretically applied flurazepam consistently potentiated the conductance increase produced by iontophoretically applied GABA in CA1 and CA3 pyramidal neurons in rat hippocampus. It is concluded that GABAergic neurotransmission has a special role in the neurophysiology of anxiety. Since anxiety is involved in the etiology of alcoholism, and since chronic ethanol intake decreases GABA levels and alters the density of GABA receptors, the findings are consistent with the hypothesis that GABAergic mechanisms may be involved in the etiology of alcoholism. (Journal abstract modified)

002841 Nistri, A. Dept. of Pharmacology, St. Bartholomew's Hospital Medical College, Charterhouse Square, London EC1M 6BQ, England **Excitatory and inhibitory actions of ibotenic acid on frog spinal motoneurones in vitro.** Brain Research. 208(2):397-408, 1981.

Ibotenic acid (IBO), a conformationally restricted analogue of the putative excitatory transmitter glutamate, was found to produce biphasic effects on frog spinal motoneurons recorded with DC coupled Ag/AgCl electrodes placed on the central end of ventral roots. The initial effect consisted of a motoneuronal depolarization with an increase in exitability tested with low intensity dorsal root stimulation (the depolarizing activity of IBO was about six times greater than that of glutamate). On washout, the depolarizing effect of IBO subsided and complete motoneuronal repolarization occurred; however, motoneuronal responses to glutamate and to transsynaptic stimulation remained depressed for prolonged periods. This depressant effect was not reproduced following prolonged administrations of depolarizing doses of glutamate but it was similar to that produced by muscimol, an agonist on inhibitory GABA receptors. Unlike the muscimol evoked depression, the IBO induced depression was insensitive to bicuculline and was antagonized by local anesthetics or high Mg2 solutions. It is suggested that a substantial part of the IBO depressant action is likely due to release of long acting inhibitory transmitters onto motoneurons. 21 references. (Author abstract)

002842 Nock, Bruce; Blaustein, Jeffrey D.; Feder, Harvey H. Institute of Animal Behavior, Rutgers University, Newark, NJ 07102 **Changes in noradrenergic transmission alter the concentration of cytoplasmic progestin receptors in hypothalamus.** Brain Research. 207(2):371-396, 1981.

A series of experiments designed to determine whether drug induced changes in NA transmission affect lordosis behavior of female guinea-pigs by altering steroid action within hypothalamic target cells is described. The effects of the dopamine-beta-hydroxylase inhibitor, U-14,624, on cytoplasmic progestin receptors in hypothalamus, preoptic area, cerebral cortex, and midbrain of estradiol benzoate primed females were examined. Results support the notion that the modulation of target tissue responsiveness to steriods is an important mechanism by which neurotransmitters affect steroid dependent processes. The operation of such a mechanisms would provide a rapid means by which environmental, behavioral, and emotional events could modulate steroid dependent behaviors and anterior pituitary function. 61 references. (Author abstract modified)

002843 Norris, P. J.; Smith, C. C. T.; De Belleroche, J.; Bradford, H. F.; Mantle, P. G.; Thomas, A. J.; Penny, R. H. C. Bradford: Dept. of Biochemistry, Imperial College of Science, London SW7 2AZ, England **Actions of tremorgenic fungal toxins on neurotransmitter release.** Journal of Neurochemistry. 34(1):33-42, 1980.

The neurochemical effects of the tremorgenic mycotoxins Verruculogen and Penitrem-A were studied in sheep and rat synaptosomes. The toxins were administered by chronic feeding to sheep and by i.p. injection to rats, and synaptosomes were prepared from cerebrocortical and spinal cord/medullary regions of rat and corpus striatum of sheep. Results indicated that both toxins interfere with amino acid neurotransmitter release mechanisms. Penitrem-A enhanced spontaneous release of glutamate, aspartate, and GABA, but reduced stimulus evoked release of these amino acids. Verruculogen enhanced spontaneous release of glutamate and aspartate from cortical synaptosomes without altering release induced by veratrine. 19 references. (Author abstract modified)

002844 Oana, Yasunori; Arai, Motoo; Miura, Shiroe. Dept. of Psychiatry, Tokyo Medical College, Tokyo, Japan **A study on effects of antiepileptic drugs upon the hippocampal afterdischarge.** Psychiatria et Neurologia Japonica. 82(1):48-66, 1980.

The effects of the four anticonvulsants phenobarbital, phenytoin, trimethadione, and carbamazepine on the hoppocampal afterdischarge were studied. Ss were 16 cats with electrodes chronically implanted by a constant current simulator. The five categories focused on include: threshold; duration; wave patterns of hippocampal after discharge; behavioral reaction; and generalized convulsions. With the exception of trimethadione, all the anticonvulsants had a similar effect on the hippocampal afterdischarge: lowering the threshold, shortening the duration, lowering spike voltage, suppressing the behavioral reaction, and suppressing convulsions. It is concluded that the main action of the anticonvulsants was not only the suppression of seizure discharge, but also the suppression of seizure discharge propagation from various areas of the brain to the peripheral motor system. 45 references. (Author abstract modified)

002845 Ohmiya, Yoshio; Mehendale, Harihara M. Mehendale: Dept. of Pharmacology and Toxicology, University of Mississippi Medical Center, 2500 North State St., Jackson, MS 39216 **Pulmonary metabolism of imipramine in the rat and rabbit: comparison with hepatic metabolism.** Pharmacology. 22(3):172-182, 1981.

The pulmonary metabolism of imipramine (IMP) was studied in male Sprague-Dawley rats and New Zealand white rabbits. The IMP metabolizing activity of rat lung was considerably greater than that of rabbit lung. The major metabolite produced by rat lung was IMP-N-oxide. The liver/lung ratio of IMP metabolizing activity varied with substrate concentrations used, indicating the unreliability of such ratios as indices of the relative contribution of the lung to drug metabolism. IMP N-oxidation by lung tissue was mediated by a noncytochrome P-450 system. 34 references. (Author abstract modified)

002846 Okamoto, Koichi; Sakai, Yutaka. Dept. of Pharmacology, National Defense Medical College, 525 Tokorozawa, Saitama 359, Japan **Inhibitory actions of taurocyamine, hypotaurine, homotaurine, taurine and GABA on spike discharges of Purkinje cells, and localization of sensitive sites, in guinea pig cerebellar slices.** Brain Research. 206(2):371-386, 1981.

The effects of the possible metabolites of taurine (taurocyamine and hypotaurine) and of homotaurine on spike discharge frequency of guinea-pig cerebellar Purkinje cells were investigated in comparison with taurine and GABA. Taurocyamine, hypotaurine, and homotaurine all dose dependently suppressed the spike frequency with potencies relative to taurine of 6, 0.5, and 500, respectively. Both picrotoxin and strychnine competitively blocked the inhibition by all the substances tested, except for the noncompetitive antagonism by picrotoxin on taurocyamine. The sites sensitive to taurocyamine and hypotaurine were situated primarily in the dendritic region of the cerebellar molecular layer, while those to homotaurine were primarily near the Purkinje cell soma. The onset of the inhibitory action of taurine and related sulfur containing substances was found to be slower than that of GABA. 24 references. (Author abstract modified)

002847 Olpe, Hans-Rudolf. Biology Research Laboratory, Pharmaceuticals Div., Ciba-Geigy Ltd. Basle, Switzerland **Differential effects of clomipramine and clorgyline on the sensitivity of cortical neurons to serotonin: effect of chronic treatment.** European Journal of Pharmacology. 69(3):375-377, 1981.

The sensitivity of rostral and cingulate cortical neurons to microiontophoretically applied serotonin (5-HT) was significantly reduced in male Tif:RAIf rats treated chronically with clorgyline (0.3mg/kg i.p. for 10 days). No change in cortical sensitivity to 5-HT was observed in rats treated chronically with clomipramine (10mg/kg i.p for 4 weeks). These findings are consistent with biochemical studies showing a decrease in 5-HT receptors after chronic treatment with clorgyline, but not after chronic treatment with clomipramine. 8 references. (Author abstract modified)

002848 Olsen, Richard W.; Leeb-Lundberg, Frederick. Division of Biomedical Sciences, University of California, Riverside, CA 92521 **Convulsant and anticonvulsant drug binding sites related to GABA-regulated chloride ion channels.** Advances in Biochemical Psychopharmacology. 26:93-102, 1981.

Radioactive drug binding studies of mammalian brain in vitro, which indicate that two classes of drug receptor sites (for picrotoxin like convulsants and barbiturates and for benzodiazepines) are related to many of the pharmacological actions of these drugs and which suggest that these receptors are coupled to the postsynaptic membrane GABA receptor/chloride ion channel complex, are summarized. A hypothetical model of the GABA receptor/Chloride ion channel complex, which incorporates three drug receptors (GABA, picrotoxin/barbiturates, and benzodiazepine) and the functional portion of the system, the chloride ion channel, is proposed. It is speculated that this system and its associated endogenous ligands are intimately involved in nervous system structures related to excitability control and seizure disorders, and possibly related to sleep and anxiety. 40 references.

002849 Ortega-Bevia, F.; Gonzalez-Vilches, J.; Fernandez, R. Depto. de Psiquiatria y Psicologia Medica, Facultad de Medicina, Universidad de Sevilla, Sevilla, Spain **/Neuroleptic action on hepatic enzymatic activity./** Accion de los neurolepticos sobre la actividad enzimatica hepatica. Actas Luso-Espanolas de Neurologia, Psiquiatria etc. 8(2):51-58, 1980.

The action of neuroleptics on hepatic biochemistry was studied. A total of 11 neuroleptics was administered orally to groups of six rats, one drug per group. Blood samples of each group were examined to determine the hepatic parenchemistry. Results show that the neuroleptics provoked an increase in serum activity in enzymatic substances and a decrease in the action of such substances in the hepatic parenchemistry. The indications for each neuroleptic drug are presented.

002850 Ortega-Bevia, F.; Gonzalez-Vilches, J.; Fernandez, R. Depto. de Psiquiatria y Psicologia Medica, Universidad de Sevilla, Sevilla, Spain **/Phenothiazine action on cerebral 5-hydroxytryptamine./** Accion de las fenotiazinas sobre la 5-HT cerebral. Revista de Psiquiatria y Psicologia Medica de Europa etc. 14(7):183-187, 1980.

A comparative analysis of the action of different phenothiazine drugs on cerebral 5-hydroxytryptamine (5-HT) was done. The change in concentration of this substance in the cerebrum of rats was studied experimentally. Results show that the intensity of the specific action of the different phenothiazines on 5-HT is not related to the particular group of drugs. Some of the drugs are more effective as antipsychotic drugs. (Journal abstract modified)

002851 Ortega-Bevia, F.; Gonzalez-Vilches, J.; Fernandez, R. Depto. de Psiquiatria y Psicologia Medica, Universidad de Sevilla, Sevilla, Spain **/Long-acting antipsychotic drugs and cerebral 5-hydroxytryptamine./** Antipsicoticos de accion prolongada y 5-HT cerebral. Revista de Psiquiatria y Psicologia Medica de Europa etc. 14(7):189-192, 1980.

The effect of different long-acting antipsychotic drugs on the concentration of cerebral 5-hydroxytryptamine (5-HT) in rats was studied. The drugs included chlorpromazine, pipothiazine palmitate, fluphenazine decanoate, reserpine, and pipothiazine undecylenate, all administered i.m. in 1mg dosages. Results show a greater concentration of cerebral 5-HT in all cases in comparison to the control group except for the group treated with reserpine, which had levels similar to those observed in the control group. (Journal abstract modified)

002852 Overstreet, David H.; Driscoll, Peter; Martin, James R.; Yamamura, Henry I. Martin: Behavioral Biology Lab., Swiss Federal Institute of Technology, E.T.H.Z., CH-8092 Zurich, Switzerland **Brain muscarinic cholinergic receptor binding in Roman high- and low-avoidance rats.** Psychopharmacology. 72(2):143-145, 1981.

The hypothesis that behavioral differences between Roman high avoidance (RHA/Verh) and Roman low avoidance (RLA/Verh) rats reflect differences in the number and/or affinity of brain muscarinic cholinergic receptors was investigated. The binding of the specific muscarinic antagonist 3H-quinuclidinyl benzilate to crude membrane preparations from cerebral cortex, hippocampus, and striatum was determined. There were no significant differences between the two rat lines for the number of muscarinic binding sites or the apparent dissociation constant, as determined by Scatchard analysis of the saturation isotherms. These data indicate that the behavioral differences between RHA/Verh and RLA/Verh rats cannot be accounted for by differences in the number or affinity of brain muscarinic cholinergic receptors. 24 references. (Author abstract modified)

002853 Owens, Dennis P.; Cicero, Theodore J. Cicero: Dept. of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63110 **Development of acute tolerance to the effects of naloxone on the hypothalamic-pituitary-luteinizing hormone axis in the male rat.** Journal of Pharmacology and Experimental Therapeutics. 216(1):135-141, 1981.

The acute development of tolerance to the effects of naloxone on the hypothalamic/pituitary/luteinizing hormone (LH) axis was demonstrated in the male rat. Naloxone causes rapid, dose dependent increases in serum LH levels in the male, apparently by blocking the actions of an endogenously occurring opioid peptide which normally inhibits the release of LH. It was found that naloxone pretreatment markedly reduced naloxone induced increases in serum LH after a second identical injection if the interval between the first and second injections was 2 to 4 hr. The diminished LH response to a second naloxone injection satisified the two pharmacological criteria for the establishment of tolerance: a parallel shift to the right in the dose response curve; and a reduced response to naloxone at the same brain concentration of the antagonist in tolerant vs. nontolerant rats. 37 references. (Author abstract modified)

002854 Pannier, L.; Rommelspacher, H. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, Ulmenallee 30, D-1000 Berlin 19, West Germany **Actions of tetrahydronorharmane (tetrahydro-beta-carboline) on 5-hydroxytryptamine and dopamine mediated mechanisms.** Neuropharmacology. 20(1):1-8, 1981.

The effects of neurotoxic agents or thermolytic lesions on serotonin (5-HT) dependent mechanisms were investigated in the hyperactivity syndrome test. 5-Hydroxytryptophan as well as tetrahydronorharmane (THN) evoked the syndrome in a dose dependent manner. Lesions of the raphe nuclei reduced the THN elicited activity syndrome. 6-Hydroxydopamine (6-OHDA) had no effect under the same conditions. Injection of p-chlorophenylalanine (p-CPA) caused a shift to the left of the THN curve. Following two doses of p-CPA on consecutive days, THN induced a cataleptic syndrome. Pretreatment with p-CPA as well as lesions of the raphe nuclei reduced apomorphine induced compulsive licking, indicating that the integrity of 5-HT containing neurons is required for the action of apomorphine. Licking movements were diminished by THN. Pretreatment with 6-OHDA strengthened this action of THN. The effect can be explained by an inhibition of postsynaptic dopaminergic receptors by THN which is not modulated by the stimulating action of 5-HT neurons on DA containing cells after their destruction by 6-OHDA. 39 references. (Author abstract modified)

002855 Pasantes-Morales, H.; Gamboa, A. Centro de Investigaciones en Fisiologia Celular, Universidad Nacional Autonoma de Mexico, A. P. 70-600, Mexico 20, DF, Mexico **Effect of taurine on 45Ca2 accumulation in rat brain synaptosomes.** Journal of Neurochemistry. 34(1):244-246, 1980.

The accumulation of labeled calcium ions (45Ca2) in Wistar rat cortical synaptosomes was inhibited markedly by the presence of taurine (5mM to 25mM) in the incubation medium. In synaptosomes a specific uptake system, showing the properties of a high affinity transport mechanism, was studied for taurine.

The effect of taurine was observed only in media containing bicarbonate. Beta-alanine also altered 45Ca2 accumulation, but GABA, glycine, and glutamate were inactive. Results support the postulated role of taurine in the modulation of calcium fluxes in excitable tissues. 24 references.

002856 Pasantes-Morales, H.; Salceda, R.; Lopez-Colome, A. M. Centro de Investigaciones en Fisiologia Celular, Universidad Nacional Autonoma de Mexico, Apartado Postal 70-600 Mexico 20, D.F., Mexico **The effect of colchicine and cytochalasin B on the release of taurine from the chick retina.** Journal of Neurochemistry. 34(1):172-177, 1980.

Colchicine caused a marked decrease in (35S)taurine release evoked by potassium chloride, meratridine, or glutamate in chick retina. Colchicine also decreased potassium evoked release of (3H)dopamine but not of (3H)GABA. Cytochalasin-B decreased the efflux of (35S)taurine stimulated by glutamate or veratridine, but not that evoked by potassium chloride; it suppressed the potassium evoked release of (3H)dopamine and slightly decreased that of (3H)GABA. Cytochalasin-B also produced a large increase in the spontaneous release of labeled GABA and taurine. Results suggest that GABA and taurine release from the chick retina occur through different mechanisms. 28 references. (Author abstract modified)

002857 Paul, Steven M.; Marangos, Paul J.; Skolnick, Phil. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **The benzodiazepine-GABA-chloride ionophore receptor complex: common site of minor tranquilizer action.** Biological Psychiatry. 16(3):213-229, 1981.

A review of recent research into the benzodiazepine-GABA-chloride ionophore receptor complex is presented, with focus on recent NIMH findings of drug influences on this supramolecular receptor complex. The demonstration of specific recognition sites for benzodiazepines in the mammalian CNS has altered current thinking on the mechanisms of action of the benzodiazepine, as well as the neurochemical events which are associated with anxiety. Recent studies suggest that the physiological regulation of the benzodiazepine receptor is far more complex than initially believed, and includes a functional coupling to both a GABA receptor and an associated chloride ionophore. It now appears that a number of other psychopharmacological agents, including minor tranquilizers other than the benzodiazepines, as well as several convulsants and anticonvulsants, may exert their pharmacologic effects by affecting one or more regulatory sites on the benzodiazepine receptor complex. In addition to a number of drugs, at least one endogenous, small molecular weight compound that has been isolated from the crude synaptosomal fraction of bovine cerebral cortex also appears to modulate this receptor complex. 32 references. (Author abstract modified)

002858 Pearson, S.; Nunn, P. B. Nunn: Dept. of Biochemistry, King's College London, Strand, London WC2R 2LS, England **The neurolathyrogen, beta-N-oxalyl-L-alpha,beta-diaminopropionic acid, is a potent agonist at frog spinal cord.** Brain Research. 206(1):178-182, 1981.

A neurotoxic amino acid, beta-N-oxalyl-L-alpha,beta-diaminopropionate (beta-ODAP), found in seeds of Lathyrus sativus and a possible causative agent of neurolathyrism, was found equipotent with kainate as a depolarizing agent on frog spinal cord ventral roots. The actions of kainate and beta-ODAP were pharmacologically indistinguishable, suggesting that activation of a common receptor is involved in their actions. If kainate and N-methyl-D-asparate (NMDA) receptors are present in human spinal cord, as in cat and frog spinal cord, these data may be relevant to the etiology of neurolathyrism. 16 references. (Author abstract modified)

002859 Percy, Vivienne A.; Lamm, Manja C. L.; Taljaard, Joshua J. F. MRC Neurochemistry Research Group, Dept. of Stellenbosch, P. O. Box 63, Tygerberg 7505, South Africa **Effects of delta-aminolaevulinic acid, porphobilinogen, amino acids and barbiturates on calcium accumulation by cultured neurons.** Biochemical Pharmacology. 30(6):665-666, 1981.

The effects of delta-aminolaevulinic acid (ALA), porphobilinogen (PBG), amino acids, and barbiturates on calcium accumulation by cultured neurons are described. Results indicate the PBG does not affect calcium accumulation and, although ALA previously has been shown to inhibit the K stimulated release of GABA from synaptosomal preparations, it did not affect the K stimulated influx of calcium into cultured neurons. ALA previously has been demonstrated to stimulate GABA and glutamic acid release from unstimulated synaptosomes, yet ALA did not affect calcium accumulation by cultured neurons. Results suggest that ALA exerts its effects on neurotransmitter release without altering membrane permeability to calcium ions. 23 references. (Author abstract modified)

002860 Peroutka, Stephen J.; Snyder, Solomon H. Snyder: Dept. of Neuroscience, Johns Hopkins University School of Medicine, 725 N. Wolfe St. Baltimore, MD 21205 **(3H)Mianserin: differential labeling of serotonin and histamine receptors in rat brain.** Journal of Pharmacology and Experimental Thrapeutics. 216(1):142-148, 1981.

Mianserin, a tetracyclic antidepressant which is a potent serotonin (5-HT) and histamine H1 antagonist in peripheral smooth muscle, was found to possess high affinity for 5-HT2 and histamine H1 receptor binding sites in brain membranes. By using (3H)mianserin, both 5-HT2 and histamine H1 receptors can be specifically labeled in rat cerebral cortex membranes. Simultaneous incubation of brain membranes with 300nM triprolidine or 30nM spiroperidol enables the selective labeling of 5-HT2 or histamine H1 receptors, respectively. In the guinea-pig cerebellum, (3H)mianserin exclusively labels histamine H1 receptors, since 5-HT2 sites are virtually absent in this area. 24 references. (Author abstract modified)

002861 Peroutka, Stephen J.; Snyder, Solomon H. Snyder: Dept. of Psychiatry and Behav. Sciences, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 **Two distinct serotonin receptors: regional variations in receptor binding in mammalian brain.** Brain Research. 208(2):339-347, 1981.

Regional variations in receptor binding in mammalian brain for serotonin (5-HT) agonists and antagonists were investigated. Two distinct 5-HT receptors in mammalian brain are labeled respectively with (3H)serotonin (5-HT1) and (3H)spiperone (5-HT2). In general, agonists display highest affinities for 5-HT1 while antagonists prefer 5-HT2 sites. 5-HT2 sites were estimated with (3H)spiperone, using the 5-HT2 specific antagonist cinanserin to displace binding to 5-HT2 but not dopamine receptors and sulpiride to displace (3H) spirperone from dopamine but not 5-HT receptors. The regional distribution of the two 5-HT receptors is similar in rat, guinea-pig, and bovine brain. However, the regional patterns of 5-HT1 and 5-HT2 receptors differ considerably in all three species. 12 references. (Author abstract modified)

002862 Peterson, S. L.; Albertson, T. E.; Stark, L. G.; Joy, R. M.; Gordon, L. S. Dept. of Pharmacology, School of Medicine, University of California at Davis, Davis, CA 95616 **Cumulative after-discharge as the principal factor in the acquisition of kindled**

seizures. Electroencephalography and Clinical Neurophysiology. 51(2):192-200, 1981.

The role of afterdischarge in the development of behavioral and electrographic seizures (kindling) was evaluated. Rats were stimulated (amygdala) once daily for 10 days 30 minutes after an intraperitoneal injection of diazepam, phenobarbital, propranolol, or vehicle. Following a 10 day period to allow for drug elimination, the daily stimulations (without drug) resumed until all animals responded with fully kindled seizures. Only the lowest dosage groups of diazepam and phenobarbital showed a savings in the number of stimulations to kindle in the nondrug state. This suggests that little or no kindling development had occurred in the drug state with the high doses. As an alternative measure of kindling, the number of seconds of cortical afterdischarge accumulated in the drug state, the nondrug state, and the grand total required to kindle were averaged and compared between the drug and control groups. No significant differences were found. Results suggest that a specific quantity of afterdischarge must be elicited to kindle (200 to 300 sec) and that any afterdischarge elicited in the presence of phenobarbital or diazepam will contribute to that quantity. 20 references. (Author abstract modified)

002863 Picotti, Giovanni B.; Carruba, Michele O.; Ravazzani, Carla; Cesura, Andrea M.; Galva, Maria D.; Da Prada, Mose. Institute of Pharmacology, School of Medicine, University of Milan, Via Vanvitelli 32, I-20129 Milano, Italy **Plasma catecholamines in rats exposed to cold: effects of ganglionic and adrenoreceptor blockade.** European Journal of Pharmacology. 69(3):321-329, 1981.

Plasma noradrenaline (NA) concentrations in male Wistar and Sprague-Dawley rats exposed to cold for 30 minutes to 24 hours were twice as high as baseline levels. Plasma adrenaline and dopamine levels were not altered by cold exposure. The cold induced increase in plasma NA concentrations in adrenalectomized animals was similar to that in intact animals. In rats given chlorisondamine to impair catecholamine release or phentolamine to impede the vasoconstrictor response, plasma adrenaline levels increased concomitantly with NA levels. Propranolol did not alter the acute neurosympathetic response to cold. 32 references. (Author abstract modified)

002864 Pohorecky, Larissa A.; Rizek, America E. Center of Alcohol Studies, Rutgers University, New Brunswick, NJ 08903 **Biochemical and behavioral effects of acute ethanol in rats at different environmental temperatures.** Psychopharmacology. 72(2):205-209, 1981.

The effects of ethanol induced hypothermia on selected biochemical and behavioral parameters were investigated in rats. Rats were kept from 1 hour preinjection to 1 hour postinjection (saline or ethanol) in an environment chamber at either 22 degrees C or 35 degrees C and then tested behaviorally or biochemically. Exposure of rats to a warm environment (35 degrees C) prevented the ethanol induced hypothermia found in rats kept at 22 degrees C. Ethanol treated rats kept at 35 degrees C had an attenuated increase in levels of free fatty acids and of corticosterone in plasma, suggesting that part of the ethanol induced response may result from hypothermia rather than from ethanol itself. In addition, tyrosine levels were unexpectedly increased by 18% in intoxicated animals kept at 35 degrees C. By contrast, gross motor activity and swim performance were impaired to a greater extent in the animals kept at 35 degrees C. The greater behavioral impairment was not due to any debilitating effects of the warm environment, since the saline control animals showed comparable activity to that of rats kept at 22 degrees C. It is concluded that ethanol induced hypothermia may influence and interact with other actions of ethanol. 32 references. (Author abstract modified)

002865 Pokorny, J.; Novakova, V.; Sterc, J. Institute of Physiology, CSAV, Videnska 1083, CS-142 20 Praha, Czechoslovakia **Bioelectrical activity of the rat brain after premature weaning and after RNA administration.** Activitas Nervosa Superior. 22(4):254-263, 1980.

Bioelectrical activity in the rat brain was studied after premature weaning and after RNA administration. Male rats prematurely weaned on the 15th day exhibited an increase in seizure susceptibility in the septum, hypothalamus, and hippocampus, when tested in adulthood. The resting EEG of these animals exhibited characteristic changes in the EEG spectrum power density by shifts in the power of individual frequencies. The administration of RNA to adult prematurely weaned animals affected, in all structures under study, the seizure susceptibility as well as the resting EEG, having caused in septum and hippocampus the return to values found in normally weaned rats. In hypothalamus, the administration of RNA also partially normalized the EEG. 21 references. (Author abstract modified)

002866 Post, Robert M.; Lockfeld, Alexandre; Squillace, Kathleen M.; Contel, Nancy R. Section on Psychobiology, Biological Psychiatry Branch, NIMH, Building 10, Room 3S239, Bethesda, MD 20205 **Drug-environment interaction: context dependency of cocaine-induced behavioral sensitization.** Life Sciences. 28(7):755-760, 1981.

The effect of the environmental context in which rats received cocaine upon subsequent cocaine induced hyperactivity and stereotypy was explored. Cocaine test cage animals were injected with cocaine in the test cage and then received saline upon leaving it 40 min later, while in the saline test cage group, the injections were in the reverse order. Thus, all animals had identical injections, handling, and environmental exposure, differing only in whether they received cocaine during or after their test cage experience. The cocaine test cage animals displayed increasing response to the 10 daily cocaine injections, i.e., behavioral sensitization. However, in contrast, the saline test cage animals had significantly less cocaine induced activation upon two of three challenges with cocaine and showed no significant evidence of behavioral sensitization even though they had received the same dose and number of previous cocaine injections in a different environment. Thus, this study reveals environment specific drug effects and suggests that environmental context plays a role in the development and manifestation of behavioral sensitization to cocaine. 22 references. (Author abstract)

002867 Pradhan, Sikta; Alphs, L.; Lovenberg, W. Section of Biochemical Pharmacology, Hypertension-Endocrine Branch, NHLBI, NIH, Bethesda, MD 20205 **Characterization of haloperidol-mediated effects on rat striatal tyrosine hydroxylase.** Neuropharmacology 20(2):149-154, 1981.

Short-term treatment of male Sprague-Dawley rats with haloperidol altered the affinity of striatal tyrosine hydroxylase (TH) for cofactor. These drugs effects were more prominent at pH 6.0 to 6.6 than at the pH optimum for striatal TH (5.8 to 6.0). Tolerance to the effects of haloperidol was apparent 2 weeks after the 10 day haloperidol treatment was terminated. 18 references. (Author abstract modified)

002868 Prakash, Madhavi Ratnam; Baouer, Najma Zaheer. Baouer: School of Life Sciences, Jawaharlal Nehru University, New Mehrauli Road, New Delhi 110067, India **Inhibition of gamma-aminobutyric acid transaminase with 6-aminonicotinamide**

in regions of the rat brain. Biochemical Pharmacology. 30(6):663-664, 1981.

The effects of 6-aminonicotinamide (6-AN) on gamma-aminobutyric acid transaminase (GABA-T) were studied in three regions of the rat brain. GABA-T activity was significantly decreased in cerebral hemispheres, cerebellum, and brainstem after 4 hours of drug treatment. Enzyme activity returned to control values in cerebral hemispheres and brainstem after 16 hours of drug treatment. In the cerebellum, however, GABA-T activity increased above control values by 41% at 16 hours. 6-AN appears to affect the GABA shunt and may be useful in studying this pathway in the CNS. 14 references. (Author abstract modified)

002869 Pycock, C. J.; Carter, C. J.; Kerwin, R. W. Dept. of Pharmacology, Medical School, University of Bristol, Bristol, BS8 1TD, England **Effect of 6-hydroxydopamine lesions of the medial prefrontal cortex on neurotransmitter systems in subcortical sites in the rat.** Journal of Neurochemistry. 34(1):91-99, 1980.

The effect of lesions of catecholamine nerve terminals in the medial prefrontal cortex of the male Porton rat on neurotransmitter mechanisms in the basal ganglia were studied. Bilateral 6-hydroxydopamine lesions were placed stereotaxically in animals pretreated with desmethylimipramine. The lesion produced a selective reduction of noradrenaline and dopamine from the medial prefrontal cortex and a decrease in tyrosine hydroxylase activity in this region. Dopmamine turnover and use in striatal and limbic regions were enhanced. Subcortical tyrosine hydroxylase activity was not altered. GABA and 5-hydroxytryptamine levels and glutamate decarboxylase and choline acetyltransferase activities were decreased in certain regions of the basal ganglia. Results suggest that frontal cortical catecholamine systems may regulate various neurotransmitter mechanisms in the basal ganglia. 38 references. (Author abstract modified)

002870 Quik, M.; Smith, P. A.; Padjen, A. L.; Collier, B. Dept. of Pharmacology, McIntyre Medical Building, McGill University, 3655 Drummond St., Montreal, Quebec H3G 1Y6, Canada **A critical evaluation of the use of toxins from dendroaspis viridis to block nicotinic responses at central and ganglionic synapses.** Brain Research. 209(1):129-143, 1981.

The use of toxins from Dendroaspis viridis to block nicotinic responses at central and ganglionic synapses is critically evaluated. Dendroaspis viridis venom was fractionated into its toxin components. Only one of the fractions possessed activity as assessed by: 1) inhibition of alpha-bungarotoxin (alpha-BGT) binding at the neuromuscular junction; or 2) inhibition of the ventral root/dorsal root potential (VR/DRP), a nicotinic response in frog spinal cord. However, in the spinal cord preparation, in addition to this blockade of the nicotinic pathway, convulsant activity and an increase in the amplitude of other root potentials was observed. Binding experiments using 125I dendrotoxin demonstrated that the labeled compound bound to CNS tissue such as brain or spinal cord; this was not displaced by nicotine or D-tubocurarine, a nicotinic antagonist, indicating either nonspecific binding or binding to a nonnicotinic receptor. These results suggest that toxins from Dendroaspis viridis venom are not suitable ligands for central nicotinic receptors. In addition, since dendrotoxins do not block cholinergic transmission in frog sympathetic ganglia, their use at ganglionic nicotinic receptors is contraindicated. 29 references. (Author abstract modified)

002871 Ragavan, Vanaja V.; Frantz, Andrew G. Dept. of Medicine, Columbia University College of Physicians and Surgeons, 630 West 168th St., New York, NY 10032 **Suppression of serum prolactin by naloxone but not by anti-beta-endorphin antiserum in stressed and unstressed rats.** Life Sciences. 28(8):921-929, 1981.

The role of endogenous opioids in the regulation of tonic and stress induced prolactin (PRL) secretion was studied in male rats. Animals with chronically indwelling intraatrial catheters were used and served as their own controls. Intravenous injection of a potent rabbit anti-beta-endorphin antiserum produced no change in either baseline serum PRL or in the rise induced by swimming for 15 min at 20 C. Naloxone produced a small but significant lowering of baseline serum PRL levels, as well as a mild blunting of the stress induced serum prolactin rise. The failure of anti-beta-endorphin antiserum to affect serum PRL may be explained either by failure of the antiserum to gain access to hypothalamic PRL regulating loci, or to lack of involvement of beta-endorphin in the control of serum PRL. The suppression of prolactin secretion seen with naloxone indicates that endogenous opioids are involved in prolactin regulation, though the relatively small magnitude of the changes observed suggests that their role under physiological conditions may be a minor one. 44 references. (Author abstract)

002872 Ravizza, L.; Bogetto, F.; Torre, E.; Rebaudengo, P. Istituto di Clinica Psichiatrica, Universita di Torino, Torino, Italy **/Norepinephrine and dopamine cerebral levels after chronic treatment with nomifensine./** Livelli di NE e DA cerebrali dopo trattamento cronico con nomifensina. Minerva Psichiatrica. 21(1):55-56, 1980.

Cerebral levels of norepinephrine (NE) and dopamine (DA) were studied in rats after treatment with nomifensine. A group of six albino Wistar rats were administered 10mg/kg for a period of 10 days. A control group received a placebo. The NE and DA levels were measured. Results show a statistically significant increase of both levels in the experimental group. The data are compared to similar research found in the literature. 4 references. (Journal abstract modified)

002873 Ravizza, L.; Torre, E.; Bogetto, F.; Rebaudengo, P. Istituto di Clinica Psichiatrica, Universita di Torino, Torino, Italy **/Acute action of nomifensine on norepinephrine and dopamine levels in the rat brain./** Azione acuta della nomifensina sui livelli di NE e DA del cervello di ratto. Minerva Psichiatrica. 21(1):45-47, 1980.

The action of nomifensine on the norepinephrine (NE), dopamine (DA), and 5-hydroxytryptamine (5-HT) cerebral levels in rats was studied. The experimental group (12 rats) was administered nomifensine in a dosage of 20mg/kg; the control group was not administered any drug. The DA, NE, and 5-HTR levels were measured in both groups. Results show that in the experimental group the DA level decreased significantly, while the NE level showed no significant variation. These results are compared to similar research studies. 11 references. (Journal abstract modified)

002874 Regan, John W.; Yamamura, Henry I.; Yamada, Shizuo; Roeske, William R. Roeske: Dept. of Internal Medicine, University of Arizona, Health Sciences Center, Tucson, AZ 85724 **High affinity renal (3H)flunitrazepam binding: characterization, localization, and alteration in hypertension.** Life Sciences. 28(9):991-998, 1981.

The binding of (3H)flunitrazepam was studied in membranes prepared from the kidney and cerebral cortex of unilaterally nephrectomized rats made hypertensive by simultaneous deoxycorticosterone acetate (DOCA) and NaCl administration. A significant increase (35% to 43%) in the number of (3H)flunitrazepam binding sites was found in the renal membranes prepared from the hypertensive rats; there was no change in the density of binding sites in the membranes obtained from the cerebral cortex. Drug specificity studies with renal membranes show that the inhibition of (3H)flunitrazepam binding by various benzodiazepines is not correlated with their pharmacologic potency as anxiolytic agents. The evidence that the renal benzodiazepine binding site is of high affinity, is specific, has a unique distribution, and is regulated during hypertension suggests that it may be associated with an important pathophysiologic structure. 21 references. (Author abstract modified)

002875 Rehavi, Moshe; Ramot, Orly; Yavetz, Bella; Sokolovsky, Mordechai. Sokolovsky: Dept. of Biochemistry, George S. Wise Faculty of Life Sciences, Tel-Aviv University, Tel-Aviv, Israel **Amitriptyline: long-term treatment elevates alpha-adrenergic and muscarinic receptor binding in mouse brain.** Brain Research. 194(2):443-453, 1980.

Alpha-adrenergic, muscarinic, and dopaminergic receptor binding in male ICR mouse brain was not altered by treatment with amitriptyline for 7 or 14 days. After 21 days of treatment with the tricyclic antidepressant, however, a twofold increase in alpha-adrenergic binding and a moderate (25%) increase in muscarinic receptor binding were detected in the medulla pons and hippocampus. No change in dopaminergic receptor binding was detected. Scatchard analysis showed that the increases in receptor density were not the result of changes in dissociation constants of tritiated ligands for their receptors. It is suggested that the increases in alpha-adrenergic and muscarinic binding were due to chronic blockade of these two types of receptors by amitriptyline. 33 references. (Author abstract modified)

002876 Roquebert, Jacques; Demichel, Patricia. Laboratoire de Pharmacodynamie, U.E.R. de Pharmacie Universite de Bordeaux II, 3 place de la Victoire, F-33000 Bordeaux, France **Calcium antagonism of the inhibitory effects of fentanyl on the contraction of the nictitating membrane in cats.** European Journal of Pharmacology. 70(1):87-90, 1981.

The contractile responses elicited from the nictitating membrane of cats by postganglionic sympathetic nerve stimulation were decreased by fentanyl (10 to 20mcg/kg injected in the lingual artery). Fentanyl (10 to 25mcg/kg) did not alter the contractile responses to noradrenaline and tyramine. The inhibitory effect of fentanyl was antagonized by naloxone. Increases in plasma calcium concentration did not alter the contractile response to sympathetic nerve stimulation, but antagonized the inhibitory effect of fentanyl in a dose dependent manner. 7 references. (Author abstract modified)

002877 Rotrosen, John; Stanley, Michael; Lautin, Andrew; Wazer, David; Gershon, Samuel. New York Veterans Administration Medical Center, New York, NY **Discrimination of functionally heterogeneous receptor subpopulations: antipsychotic and antidopaminergic properties of metoclopramide.** Psychopharmacology Bulletin. 17(1):110-113, 1981.

The discrimination of functionally heterogeneous receptor subpopulations by metoclopramide, a substituted benzamide derivative which is structurally similar to procainamide and sulpiride, is described. In a series of projects designed to evaluate the relevancy and role of dopamine (DA) binding sites and adenylate cyclase coupled DA receptors as mediators of antidopamine effects and antipsychotic activity, metoclopramide effects were studied. It is proposed that a subpopulation of DA/neuroleptic binding sites represents the receptors that are funcitonally important as mediators of DA antagonisms in general, and metoclopramide's action in particular. Metoclopramide differs from other DA antagonists insofar as it displays specificity for these relevant sites, but not for numerous others. 12 references. (Author abstract modified)

002878 Rumigny, Jean-Francois; Maitre, Michel; Recasens, Max; Blindermann, Jean-Marc; Mandel, Paul. Centre de Neurochimie du CNRS and INSERM 44, Faculte de Medecine, 11 rue Humann, F-67085 Strasbourg Cedex, France **Multiple effects of repeated administration of gamma-acetylenic GABA on rat brain metabolism.** Biochemical Pharmacology. 30(4):305-312, 1981.

The effects of chronic injections of gamma-acetylenic GABA on some parameters of rat behavior and cerebral amino acid metabolism are presented. When 4-amino-hex-5-ynoic acid, the acetylenic analogue of GABA, is given chronically to rats over a period of 8 days, several biochemical modifications are found in the brain. The following enzymatic activities are severely affected: GABA-transaminase (GABA-T), glutamate decarboxylase (GAD), alanine aminotransferase (Ala-T), and to a lesser extent glutamate oxaloacetate transaminase (GOT) and cystein sylphinate transaminase (CSA-T). The drug does not appear to interfere with pyridoxal phosphate synthesis. Increases in cerebral GABA, glutamate, alanine, phenylalanine, ornithine, and taurine levels were observed. There were no changes in the levels of GAD and GABA-T apoenzymes despite a chronic increase in the brain GABA level. These biochemical alterations are accompanied by behavioral changes including grand mal like seizures and a modification of feeding activity. Considering the multiple biochemical effects of the drug, these behavioral changes are probably not related to a specific alteration in GABA metabolism. 42 references. (Author abstract modified)

002879 Rylett, B. Jane; Colhoun, E. Howard. Colhoun: Dept. of Pharmacology, University of Western Ontario, London, Ontario, Canada N6A 5C1 **Kinetic data on the inhibition of high-affinity choline transport into rat forebrain synaptosomes by choline-like compounds and nitrogen mustard analogues.** Journal of Neurochemistry. 34(3):713-719, 1980.

Choline analogues and nitrogen mustard derivatives were evaluated as inhibitors of high affinity transport of choline in female Sprague-Dawley rat forebrain synaptosomes. When synaptosomes were preincubated for 10 minutes with choline mustard aziridinium ion, monoethylcholine, and monoethylcholine mustard aziridinium ion, the agents appeared to be equipotent as inhibitors of high affinity uptake. Acetylcholine mustard aziridinium ion was less potent than these compounds, but more potent than ethoxycholine and ethoxycholine mustard aziridinium ion. High affinity choline transport mechanisms were specific for hydroxylated compounds over those in which the hydroxyl had been acetylated and removal of the carbonyl oxygen of the acetylated analogues decreased affinity another 20-fold. The aziridinium ring on the nitrogen of the mustard analogues was important in determining the extent of reversibility of the binding of these agents to the carrier protein. It is concluded that the mustard analogues may be potent alkylators of the high affinity choline carrier and, therefore, agents in monitoring acetylcholine turnover in systems where the carrier is blocked. 57 references. (Author abstract modified)

002880 Saller, Charles F.; Chiodo, Louis A. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Glucose suppresses basal firing and haloperidol-induced increases in the firing rate of central dopaminergic neurons.** Science. 210(4475):1269-1271, 1980.

In the rat, doses of glucose sufficient to raise glucose concentrations in the blood to levels equivalent to those produced by a meal or stress are reported to suppress the firing of dopamine containing neurons located within the substantia nigra. Glucose also prevented or reversed the increase in discharge rate of dopaminergic cells normally elicited by the antipsychotic agent haloperidol. Fructose did not change the discharge rates of dopaminergic cells. It is suggested that daily physiological fluctuations in glucose availability may influence significantly dopamine mediated activity in the brain. 16 references. (Author abstract modified)

002881 Savage, Daniel Dexter, II. University of Pennsylvania **3H-serotonin binding sites in rat brain: effects of repeated administration of antidepressant drugs. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):2997-B, 1981. Ann Arbor, Univ. Microfilms No. 8028886, 176p., 1980.

The effects of repeated administration to rats of serotonin uptake inhibitors or monoamine oxidase inhibitors on serotonin receptors and serotonin concentration in rat brain was examined. Four to 16 days of repeated administration of monoamine oxidase inhibitors (MAOI) capable of inhibiting A-type monoamine oxidase caused a significant reduction in specific 3H-serotonin binding in brain. Repeated administration of inhibitors of B-type monoamine oxidase had no effect on specific 3H-serotonin binding. In contrast to the MAOIs, the repeated administration of serotonin uptake inhibitors had no effect on specific 3H-serotonin binding sites. The relationships between changes in 3H-serotonin binding and changes in brain serotonin concentration in response to repeated administration of MAOIs was examined. The effect of MAOIs on serotonin receptor sites appears to be mediated indirectly by the MAOIs interfering with the metabolism of serotonin and leading to an increased exposure of serotonin receptors to serotonin. (Journal abstract modified)

002882 Sawynok, Jana; Labella, Frank S. Dept. of Pharmacology and Therapeutics, University of Manitoba, 770 Bannatyne Ave., Winnipeg, Manitoba, Canada R3E OW3 **GABA and baclofen potentiate the K-evoked release of methionine-enkephalin from rat striatal slices.** European Journal of Pharmacology. 70(2):103-110, 1981.

GABA potentiated the potassium (K) evoked release of methionine-enkephalin (ME) from slices of male Sprague-Dawley rat corpus striatum, but only when a submaximal concentration (30mM) of K was used. The effect of GABA was dose dependent between 100 and 1000mcM; at these concentrations, GABA did not alter basal release of ME. The effect of GABA on evoked release of ME was mimicked by both isomers of baclofen, but not by muscimol. Ficrotoxin (100mcM) blocked the enhancement of ME release by GABA and baclofen. Bicuculline methiodine (100mcM) did not block the effect of GABA. The effect of GABA on ME release maybe mediated by an atypical GABA receptor which is activated by baclofen. 50 references. (Author abstract modified)

002883 Schatz, Robert A.; Stramentinoli, Giorgio; Sellinger, Otto Z. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Decreased cerebral catabolism of (3H)histamine in vivo after S-adenosylmethionine administration.** Journal of Pharmacology and Experimental Therapeutics. 216(1):118-124, 1981.

Decreased cerebral catabolism of (3H)histamine in vivo after administration of S-adenosyl-L-methionine (SAM) is described. Brains of SAM treated mice contained more (3H)histamine than vehicle treated controls at 20 sec, 2, 5, and 10 min. (3H)methylhistamine (MeHA) levels were lower than controls at 20 sec, but higher at 2 and 5 min. Fifteen min after intraventricular (3H)histidine, brains of SAM treated mice contained 47% more (3H)histimine and 39% more (3H)MeHA, while (3H)histidine and (3H)methylimidazoleacetic acid levels remained unchanged. In vitro, SAM had no effect on monoamine oxidase type-A or type-B. Thse findings demonstrate that the rate of catabolism of histamine to MeHA is significantly decelerated in brains containing elevated levels of SAM. 74 references. (Author abstract modified)

002884 Schultz, J. E.; Siggins, G. R.; Schocker, F. W.; Turck, M.; Bloom, F. E. Bloom: Arthur V. Davis Center for Behavioral Neurobiology, Salk Institute, P.O. Box 85800, San Diego, CA 92138 **Effects of prolonged treatment with lithium and tricyclic antidepressants on discharge frequency, norepinephrine responses and beta receptor binding in rat cerebellum: electrophysiological and biochemical comparison.** Journal of Pharmacology and Experimental Therapeutics. 216(1):28-38, 1981.

The prolonged actions of desipramine (DMI), imipramine,and lithium chloride (Li) were compared in electrophysiological and biochemical tests on rat cerebellum. Cerebellar Purkinje cells were studied by electrophysiological and iontophoretic techniques and cerebellar slices and homogenates were assessed in vitro for changes in beta receptor binding and responsitivity of the cyclic AMP system to norepinephrine (NE). Prolonged treatment with DMI or Li was found to produce changes in noradrenergic responsivity of cerebellar Purkinje neurons which are opposite to the effects of these drugs applied acutely by iontophoresis. These results provide electrophysiological evidence for reciprocal adaptive changes in NE sensitivity after chronic treatment with antidepressant drugs. 54 references. (Author abstract modified)

002885 Schulz, David W.; MacDonald, Robert L. Neurosciences Program, University of Michigan, Ann Arbor, MI 48109 **Barbiturate enhancement of GABA-mediated inhibition and activation of chloride ion conductance: correlation with anticonvulsant and anesthetic actions.** Brain Research. 209(1):177-188, 1981.

The anesthetic/sedative barbiturate pentobarbital (PB) and the anticonvulsant barbiturate phenobarbital (PhB) were applied to mammalian spinal cord neurons in primary dissociated cell culture to assess their effects on: 1) postsynaptic GABA responses; 2) paroxysmal activity produced by the convulsant bicuculline; 3) resting membrane properties; and 4) spontaneous neuronal activity. Results demonstrate that: 1) anticonvulsant actions occurred at barbiturate concentrations which augmented GABA responses; 2) anesthetic actions occurred at barbiturate concentrations which produced direct increases in chloride conductance; 3) both anticonvulsant and anesthetic actions occurred at clinically relevant concentrations; and 4) concentrations of PhB, but not PB, which produced GABA augmentation and direct conductance changes were widely separated. These findings support the hypotheses that augmentation of GABA mediated inhibition and possibly reduction of glutamate (GLU) mediated excitation form the basis at least in part for barbiturate anticonvulsant action and that addition of direct increases in chloride conductance to augmentation of GABA mediated inhibition and reduction of GLU mediated excitation may partially underlie anesthetic/sedative barbiturate action. 31 references. (Author abstract)

002886 Schwindt, P. C.; Crill, W. E. Seattle V. A. Medical Center, Seattle, WA 98108 **Voltage clamp study of cat spinal motoneurons during strychnine-induced seizures.** Brain Research. 204(1):226-230, 1981.

Cat spinal motoneurons were examined during strychnine induced spinal seizures by the technique of somatic voltage clamp. No clear alteration of voltage dependent ionic currents was required for typical strychnine induced paroxysmal depolarization shifts (PDSs) to develop in contrast to results previously obtained during penicillin induced spinal seizures. Voltage clamp of evoked and spontaneous PDSs indicates these are generated by a synchronized mixture of excitatory and inhibitory synaptic currents with excitation predominating. 15 references. (Author abstract modified)

002887 Sellinger, Otto Z.; Dietz, Dennis D. Laboratory of Neurochemistry, Mental Health Research Institute, University of Michigan Medical Center, Ann Arbor, MI 48109 **The metabolism of 5-hydroxytryptamine in the methionine sulfoximine epileptogenic rat brain.** Journal of Pharmacology and Experimental Therapeutics. 216(1):77-82, 1981.

The effects of the slow acting convulsant agent L-methionine-dl-sulfoximine (MSO) on regional metabolism of cerebral 5-hydroxytryptamine (5-HT) were investigated. Results include: 1) 5-HT levels in brainstem, midbrain, hippocampus and cortex, and 5-hydroxyindoleacetic acid (5-HIAA) levels in the cortex and midbrain were decreased following a single dose of MSO; 2) pretreatment with MSO plus p-chlorophenylalanine caused a greater reduction of 5-HT levels in the midbrain and the hypothalamus than was noted after p-chlorophenylalanine alone; 3) pretreatment with MSO antagonized the elevation of 5-HT levels noted in the brainstem and the cortex 30 min after the administration of clorgyline, an inhibitor of monoamine oxidase, type-A; 4) pretreatment with MSO antagonized the reduction of 5-HIAA levels noted in the cortex and in the striatum after the administration of clorgyline; and 5) pretreatment with MSO also led to a significant reduction of the formation of (14C)5-HT from intraaterially administered (14C)5-hydroxytryptophan initially in the brainstem and subsequently in the striatum. It is suggested that MSO elicited, time dependent, regional perturbations of 5-HT metabolism mediate the desynchronization of the firing rates of inhibitory serotonergic fibers, and thus help to create the MSO epileptogenic state. 34 references. (Author abstract modified)

002888 Sharif, Najam A.; Roberts, Peter J. Roberts: Dept. of Physiology and Pharmacology, University of Southampton, Southampton S09 3TU, England **Effects of protein- and membrane-modifying agents on the binding of L-(3H)glutamate to cerebellar synaptic membranes.** Brain Research. 194(2):594-597, 1980.

The specific binding of L-(3H)glutamate to cerebellar synaptic membranes was modified by treating the membranes with proteolytic enzymes, phospholipase-A, lipid perturbants, and protein modifying reagents, and the effects of these substances on the glutamate binding were investigated. Modification of carboxyl or thiol groups increased glutamate binding, whereas oxidation, alkylation, and reduction of disulphide bonds denatured the receptor. Perturbation of protein or lipid moieties decreased binding, indicating the importance of protein/lipid interactions for the maintenance of a stable receptor conformation. 8 references.

002889 Sharpe, Lawrence G.; Pickworth, Wallace B. NIDA, Division of Research, Addiction Research Center, Lexington, KY 40583 **Pharmacologic evidence for a tonic muscarinic inhibitory input to the Edinger-Westphal nucleus in the dog.** Experimental Neurology. 71(1):176-190, 1981.

The cholinergic characteristics of the parasympathetic preganglionic cell groups controlling pupillary diameter were investigated, and pharmacologic evidence for a tonic muscarinic inhibitory input to the Edinger-Westphal nucleus in the dog was found. In the awake dog, carbachol, bethanechol, and physostigmine, but not nicotine, produced dose dependent mydriases when mirocinjected into sites within or near the Edinger-Wesphal nucleus. This cholinergic induced mydriasis was prevented by methylatropine nitrate. A muscarinic induced mydriasis appears to be due to inhibition of the pupilloconstrictor neurons because it occurs in the chonically sympathectomized and acutely decerebrated dog; and it does not correlate with sympathetic responses. 29 references. (Author abstract modified)

002890 Sharpless, Nansie S. Dept. of Psychiatry, Albert Einstein College of Medicine, Bronx, NY 10461 **Accelerated metabolism of probenecid during long-term treatment of rats with anticonvulsant drugs: effect on central serotonin turnover studies.** Neuropharmacology. 20(3):211-216, 1981.

The effect of long-term administration (once daily for 9 days) of phenytoin (50mg/kg), sodium phenobarbital (25mg/kg), primidone (50mg/kg), and L-5-hydroxytryptophan (L-5-HTP, 50mg/kg) on probenecid metabolism and on serotonin turnover rates were studied in male Sprague-Dawley rats. Chronic anticonvulsant drug treatment did not alter brain serotonin turnover. However, the rate of accumulation of 5-hydroxyindoleacetic acid (5-HIAA) in brain during the first 90 minutes after probenecid was lower in rats treated with phenobarbital than in controls. Brain 5-HIAA levels were elevated 6 hours after probenecid in rats treated with phenytoin, L-5-HTP, or vehicle, but not in those treated with phenobarbital or primidone. Serum concentrations of probenecid decreased more rapidly in rats treated with primidone or phenobarbital than in those given vehicle, L-5-HTP, or phenytoin. Results are discussed in relation to the use of probenecid induced accumulations of 5-HIAA to estimate central serotonin turnover rates. 21 references. (Author abstract modified)

002891 Shipley, J. E.; Rowland, Neil; Antelman, S. M.; Buggy, J.; Edwards, D.J.; Shapiro, A. P. Rowland: Dept. of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Increased amphetamine stereotypy and longer haloperidol catalepsy in spontaneously hypertensive rats.** Life Sciences. 28(7):745-753, 1981.

Spontaneous hypertensive rats (SHR) of both sexes and from two sources were found to exhibit enhanced stereotyped behavior following amphetamine (AMP) administration. Both the intensity and the duration of sniffing and licking were higher in SHR than in Wistar or Sprague-Dawley controls. SHR exhibited longer catalepsy after haloperidol (HAL) than did controls. Rats made hypertensive by the Goldblatt one kidney method showed neither increased AMP stereotypy nor longer HAL catalepsy. The increased effect of AMP in SHR was not due to greater drug accumulation in the brain. These findings are discussed in terms of altered brain catecholamine metabolism in SHR, and are related to experiments of chronic stress and the sensitization of AMP's effects. 34 references. (Author abstract modified)

002892 Shumilina, A. I.; Zhuravlev, B. V.; Orbachevskaya, I. Yu. Institut normal'noy fiziologii im. P. K. Anokhina AMN SSSR, Moskva, USSR **/On correlation of behavioral reactions and neuronal activity in the hypothalamus under subcutaneous gastrin injection./** O korrelyatsii povedencheskikh reaktsiy i neyronnoy aktivnosti gipotalamusa pri podkozhnom vvedenii gastrina. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 30(6):1298-1301, 1980.

The correlation of behavioral reactions and neuronal activity in the hypothalamus under subcutaneous gastrin injection was studied in two series of experiments on rabbits weighing 3 to 3.5 kg, some of which had been deprived of food for 24 hours and others of which had been fed. The animals were placed in a special chamber. In the first series of experiments their movements were restricted, but in the second series they were allowed free behavior. Pentagastrin (0.02mg/kg) was injected into the animals subcutaneously. In the course of 2 to 3 minutes the initial extracellular activity of the lateral hypothalamus was measured using glass microelectrodes. It was intensified and recorded on a magnetic tape. In the second series of experiments, pentagastrin was injected, and the activity of the same neuron was recorded during the course of 30 to 40 minutes. Results show that gastrointestinal hormones participate in the regulation of the functional system which supports the optimal level of nutritional substances in the blood. 9 references.

002893 Sieghart, W.; Placheta, P.; Supavilai, P.; Karobath, M. Psychiatrische Universitatsklinik, A-1090 Vienna, Austria **GABA receptor associated drug receptors.** Advances in Biochemical Psychopharmacology. 26:121-128, 1981.

Evidence for the molecular and pharmacological heterogeneity of the GABA/benzodiazepine receptor complex is reviewed. At least two types of GABA/benzodiazepine receptor complexes appear to exist which differ with respect to the benzodiazepine binding protein. One type of complex which contains the benzodiazepine protein P51 occurs in all brain regions. Another receptor complex contains the benzodiazepine binding protein P55 and is found in the hippocampus and other brain regions, but not in the cerebellum. This molecular heterogeneity of benzodiazepine binding proteins may be the cause of the observed differences in the modulation by GABA and pyrazolopyridines of benzodiazepine receptor binding in the cerebellum and hippocampus. Alternatively, additional differences in the molecular properties of the GABA or pyrazolopyridine recognition sites or differences in the mode of coupling of the various constituents of the receptor complex might explain the observed regional pharmacological heterogeneity of the GABA/benzodiazepine receptor complexes. 16 references.

002894 Sillito, Adam M.; Kemp, John A.; Milson, James A.; Berardi, Nicoletta. Dept. of Physiology, Medical School, Birmingham B15 2TJ, England **A re-evaluation of the mechanisms underlying simple cell orientation selectivity.** Brain Research. 194(2):517-520, 1980.

The orientation selectivity of simple cells in the cat visual cortex was lost when the GABA antagonist N-methyl bicuculline was applied iontophoretically. Receptive field dimensions were compatible with those expected from a single dorsal lateral geniculate input. Results suggest that simple cell orientation selectivity is due to the operation of an intracortical inhibitory mechanism rather than to asymmetries in excitatory input. 13 references. (Author abstract modified)

002895 Singer, Leonard; Imbs, Jean-Louis; Danion, Jean-Marie; Schmidt, Mariette; Sebban, Miryam. Centre Hospitalier Universitaire de Strasbourg, 1, place de l'hopital, F-67091 Strasbourg Cedex, France **/Influence of psychotropic drugs on the urinary elimination of lithium./** Influence des psychotropes sur l'elimination urinaire du lithium. Psychologie Medicale. 12(11):2345-2349, 1980.

The effects of psychotropic drugs on the urinary elimination of lithium were studied in the rat. The Ss were divided into two groups, control and experimental. Ss in the experimental group were administered one of four psychotropic drugs: chlorpromazine (5.7mg/kg/day), haloperidol (0.5mg/kg/day), clomipramine (2.5mg/kg/day), and carpipramine (10mg/kg/day), each for 5 days. Results indicate that the administration of chlorpromazine, haloperidol, and, to a lesser degree, clomipramine decreased tubular reabsorption of lithium. Carpipramine tended to increase tubular reabsorption of lithium and increased lithium plasma levels. These data demonstrate that lithium plasma levels must be checked when major tranquilizers or antidepressant drugs are administered to patients treated with lithium. 15 references. (Journal abstract modified)

002896 Skolnick, P.; Moncada, V.; Barker, J. L.; Paul, S. M. Lab. of Bioorganic Chemistry, National Institute of Arthritis, Metabolism and Digestive Disease, NIH, Bethesda, MD 20205 **Pentobarbital: dual actions to increase brain benzodiazepine receptor affinity.** Science. 211(4489):1448-1450, 1981.

The binding of (3H)diazepam to benzodiazepine receptors was studied in extensively washed membranes of rat cerebral cortex in the presence of the depressant barbiturate, pentobarbital. Pentobarbital, like the endogenous neurotransmitter GABA, increased the basal binding and also potentiated the GABA enhanced binding of (3H)diazepam to benzodiazepine receptors by increasing the apparent affinity of (3H)diazepam for the benzodiazepine receptors. The concentrations of pentobarbital necessary to elicit these effects in vitro were the same as those observed after treatment with pharmacologically relevant doses, suggesting that a common neurochemical association may exist between these two types of compounds. 16 references. (Author abstract)

002897 Smith, C. C. T.; Bradford, H. F.; Thompson, E. J.; MacDermot, J. Bradford: Dept. of Biochemistry, Imperial College, London SW7 2AZ, England **Actions of beta-bungarotoxin on amino acid transmitter release.** Journal of Neurochemistry. 34(3):487-494, 1980.

The effects of purified beta-bungarotoxin (5 or 10mcg/ml) on the metabolic and transmitter releasing properties of female Sprague-Dawley rat cortical synaptosomes were studied. The toxin stimulated control respiratory rates, but blocked the respiratory response to veratridine. Potassium levels were greatly reduced (54%). Release of endogenous glutamate, aspartate, and GABA was increased. The toxin inhibited the uptake of (U-14C)GABA by 35% and that of (U-14C)glutamate by 53%; this uptake inhibition was calcium dependent and was reduced by tetrodotoxin. The toxin also had a depolarizing effect at the locus neuromuscular junction. 24 references. (Author abstract modified)

002898 Smith, Craig P.; Ellis, Daniel B.; Meyerson, Laurence R. Dept. of Biochemistry, Hoechst-Roussel Pharmaceuticals, Inc., Route 202-206 North Somerville, NJ 08876 **Dopaminergic agonist and antagonist effects on striatal tyrosine hydroxylase distribution.** Life Sciences. 28(2):193-197, 1981.

Dopaminergic agonist and antagonist effects on striatal tyrosine hydroxylase (TH) distribution were investigated. Rats were decapitated 1 hour after either haloperidol or 30 min after apomorphine in the presence or absence of pyrogallol pretreatment. Subcellular fractions were prepared from striatal tissue, and L-DOPA formation was measured using reverse phase, paired ion high performance liquid chromatography with electrochemical detection. Results indicate that the in vivo administration of haloperidol, but not apomorphine, shifts the subcellular distribution of striatal TH activity. This shift occurred from the cytosol fraction to the crude mitochondrial fraction. No shift in TH activity was observed within the crude synaptosomal fraction after either drug. It is suggested that the ability of haloperidol to increase dopaminergic activity in vivo is associated with a shift in striatal TH activity distribution. 20 references. (Author abstract modified)

002899 Smith, Stephen A.; Pogson, Christopher I. Beecham Pharmaceuticals, Biosciences Research Centre, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey KT18 5XQ, England **Effects of benserazide and carbidopa on the metabolism of L-tryptophan by isolated rat liver cells.** Biochemical Pharmacology. 30(6):623-628, 1981.

The effects of two inhibitors of aromatic amino acid decarboxylase, benserazide and carbidopa, on the metabolism of L-tryptophan by liver cells prepared from 48 hours starved rats was studied. Tryptophan 2,3-dioxygenase (pyrrolase) and kynureninase activities were determined simultaneously using L-(ring 2-14C), L-(carboxyl-14C), and L-(methylene-14C)tryptophan. In hepatocytes incubated with a low physiological concentration of tryptophan, carbidopa produced a significant inhibition of kynureninase activity. The effects of benserazide were similar, but benserazide appears less potent. Neither compound influences pyruvate oxidation. Implications of these data for the research literature concerning the in vivo oxidation of tryptophan by benserazide and carbidopa are discussed. 18 references. (Author abstract modified)

002900 Sokoloff, P.; Martres, M. P.; Schwartz, J. C. Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2ter, rue d'Alesia, F-75014 Paris, France **Three classes of dopamine receptor (D-2, D-3, D-4) identified by binding studies with 3H-apomorphine and 3H-domperidone.** Naunyn-Schmiedeberg's Archives of Pharmacology. 315(2):89-102, 1980.

Two radioligands, 3H-apomorphine and 3H-domperidone, were used to study dopamine receptor subtypes in homogenates from male Sprague-Dawley rat brain. Binding sites were analyzed for drug specificity, localization, and sensitivity to guanosine triphosphate and to thermal denaturation. Results demonstrated the presence of three distinct classes of dopamine receptor in striatum and nonstriatal regions. These receptor types (D-2, D-3, and D-4) all differed from the recognition moiety of dopamine sensitive adenylate cyclase (D-1 receptor). 67 references. (Author abstract modified)

002901 Spear, Linda Patia. Department of Psychology, State University of New York at Binghamton, Binghamton, NY 13901 **A psychopharmacological approach to memory processing.** In: Thompson, R., Neural mechanisms of goal-directed behavior & learning. New York, Academic Press, 1980. 639 p. (p. 425-435).

The problem of the physiological basis of synaptic plasticity is approached from a psychopharmacological perspective. Autoreceptor hyposensitization may develop normally as a consequence of repeated utilization of synapses. Such a process may constitute a simple mechansim for stabilization of neuronal circuits repetitively activated during a learning situation. Alterations that occur at the synaptic level after chronic drug administration may be a model with which to investigate biological substrates of learning and memory processes. Chronic amphetamine administration during the retention interval seems to enhance the retention of adult rats, but not perhaps that of weanling rats whose synaptic modulatory devices are not yet mature. Use of such a psychopharmacological model in combination with neurochemical approaches may be helpful in investigations of the biological bases of learning and retention. 45 references.

002902 Speth, Robert C.; Bresolin, Nereo; Mimaki, Takashi; Deshmukh, Pushpa P.; Yamamura, Henry I. Dept. of Pharmacology and Psychiatry, University of Arizona Health Sciences Center, Tucson, AZ 85724 **Neuronal localization of benzodiazepine receptors in the murine cerebellum.** Advances in Biochemical Psychopharmacology. 26:27-39, 1981.

The localization of benzodiazepine receptors in the mouse cerebellum in the staggerer and weaver mutant mouse strains is described. Selective genetic and chemical lesions which affect specific neuronal populations in the cerebellum were studied for changes in benzodiazepine receptors. Destruction of cerebellar climbing fibers with 3-acetylpyridine, did not affect cerebellar benzodiazepine receptors. Destruction of Purkinje, basket, and stellate cells with intracerebellar kainic acid caused moderate decreases in benzodiazepine receptor density. Destruction of Purkinje cells with chronic high doses of phenytoin also caused a significant decrease in benzodiazepine receptor density. In weaver mice, benzodiazepine receptor density was unchanged, while the absolute number of benzodiazepine receptors decreased by 57%. In staggerer mice, there was a 45% decrease in benzodiazepine receptor density and a 90% decrease in the absolute number of benzodiazepine receptors. Results suggest that benzodiazepine receptors exist on cerebellar Purkinje cells, that they probably also occur on cerebellar granule cells, and that they do not appear to be present on cerebellar glial cells or on climbing fibers. 31 references. (Author abstract modified)

002903 Squires, Richard F. Rockland Research Institute, Orangeburg, NY 10962 **GABA receptors regulate the affinities of anions required for brain specific benzodiazepine binding.** Advances in Biochemical Psychopharmacology. 26:129-138, 1981.

A series of studies suggesting that GABA receptors regulate the affinities of the anions required for brain specific benzodiazepine binding is described. It is noted that beta-carboline-3-carboxylate methyl ester (BCME) discriminates between different benzodiazepine/ion/GABA receptor complexes. The available evidence suggests that there are more than two such receptor complexes. The pervasive effects of GABA mimetics on anion dependent 3H-flunitrazepam binding suggests that virtually all benzodiazepine receptors are coupled to GABA receptors. This conclusion is also supported by light microscopic autoradiographical localization of 3H-muscimol and 3H-flunitrazepam binding sites, and these studies also suggest that many GABA receptors are not coupled to benzodiazepine receptors. 24 references.

002904 Steinhauer, Hjalmar B.; Hertting, Georg. Dept. of Internal Medicine IV, University of Freiburg, D-7800 Freiburg i.Br., West Germany **Lowering of the convulsive threshold by non-steroidal anti-inflammatory drugs.** European Journal of Pharmacology. 69(2):199-203, 1981.

Nonsteroidal antiinflammatory drugs altered the convulsant threshold for pentetrazol in male NMRI mice by inhibiting cerebral synthesis of prostaglandins (PG) or thrombaxone (TX). The increases in brain PGE2, PGF2alpha, and TXB2 induced by convulsant doses of pentetrazol were inhibited by indomethacin, flurbiprofen, and diclofenac. These drugs also lowered the median lethal does (LD50) for pentetrazol and accelerated the onset of tonic seizures after pentetrazol. Ibuprofen in a submaximamly effective dose also significantly inhibited cerebral arachidonic acid metabolism and lowered the LD50 for pentetrazol. Aspirin and paracetemol were inactive in vivo. 18 references. (Author abstract modified)

002905 Sterman, Arnold B.; Spencer, Peter S. Spencer: Institute of Neurotoxicology, Dept. of Neurosciences, Albert Einstein College of Medicine, Bronx, NY 10461 **The pathogenesis of primary internodal demyelination produced by acetyl ethyl tetramethyl tetralin: evidence for preserved Schwann cell somal function.** Journal of Neuropathology and Experimental Neurology. 40(2):112-122, 1981.

The pathogenesis of primary internodal peripheral nervous system demyelination produced by acetyl ethyl tetramethyl tetralin (AETT) was studied in subchronically intoxicated rats with intact sciatic nerves (right side) and focally traumatized nerves (left side) undergoing myeline breakdown and repair. At 6 weeks and prior to onset of demyelination, Sprague-Dawley rats (n=16) treated with 50mg/kg/day AETT, dissolved in ethanol and mixed with food, showed an increase in the number of visible Schmidt-Lanterman incisures per internode of large diameter fibers in tibial nerves. By 10 weeks, the same group of fibers had begun to develop juxtanodal and internodal myelin bubbles. Subsequently, intramyelinic phagocytes of hematogenous derivation removed entire internodes of endematous myelin. A comparison of AETT treated animals and controls subjected to left hindlimb surgery indicates that responses to nerve injury were quantitatively similar for experimentals and controls at 1 to 16 weeks of AETT treatment. These results are compatible with the view that AETT damages myelin directly, that Schwann cell somal functions are not seriously affected by AETT, and that Schmidt-Lanterman incisures undergo changes prior to demyelination, which may represent a physiological response of the Schwann cell to toxic attack on this myelin sheath. In concert, findings challenge the view that primary internodal demyelination is necessarily indicative of metabolic dysfunction of the Schwann cell soma. 23 references. (Author abstract modified)

002906 Stewart, Jane; Eikelboom, Roelof. Dept. Psychology, Concordia University, 1455 de Maisonneuve Blvd., Montreal, Quebec, Canada H3G 1M8 **Interaction between the effects of stress and morphine on body temperature in rats.** Life Sciences. 28(9):1041-1045, 1981.

The relation between stress induced and morphine induced body temperature changes was examined in rats. Three groups of eight animals thoroughly habituated to handling and rectal probing, and three groups of eight experimentally naive animals were injected intraperitoneally with either 1, 5, or 30mg/kg morphine sulphate on each of 6 consecutive days. Differences in temperature readings from the preinjection baseline show that on Day 1 of the experiment, stress acted to effectively increase the potency of morphine, causing slightly increased hyperthermia at the lowest dose and greatly increased hypothermia at the highest dose. By Day 6, the differences between habituated and nonhabituated animals had disappeared. Results are discussed in terms of the interaction between the temperature changes produced by endogenous opioids in stressed animals and the actions of exogenously administered morphine. 13 references. (Author abstract modified)

002907 Stone, T. W.; Hollins, Carolyn; Lloyd, Hilary. Dept. of Physiology, St. Georges Hospital Medical School, University of London, London SW17 ORE, England **Methylxanthines modulate adenosine release from slices of cerebral cortex.** Brain Research. 207(2):421-431, 1981.

Factors affecting the release of adenosine, adenine, and GABA (including the influence of methylxanthines) were investigated in slices of mouse or rat cerebral cortex incubated with (3H)adenosine or (3H)adenine and/or (14C)GABA. Although release of purines and GABA could be induced by ouabain, or p-hydroxymercuribenzoate, no release was produced by ethacrynic acid, noradrenaline, or SC 13504. Therefore, release is probably not related to (Na,K) adenosine triphosphatase (ATPase) or Mg2-ATPase inhibition. Caffeine, theophylline, aminophylline, and isobutyl-methylxanthine markedly depressed the release of purines evoked by ouabain. Nonxanthine inhibition of phosphodiesterase had much weaker though statistically significant effects. The methylxanthines had no significant effect on GABA release. It is suggested that the results can be explained on the basis of a positive feedback system in which released adenosine activates membranal adenylate cyclase, and the increased concentration of cyclic AMP which forms the origin of much of the adenosine released subsequently. However, the existence of an intracellular receptor for methylxanthines which directly causes the inhibition of purine release cannot be excluded. 50 references. (Author abstract modified)

002908 Sugrue, Michael F. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg Cedex, France **Effects of acutely and chronically administered antidepressants on the clonidine-induced decrease in rat brain 3-methoxy-4-hydroxyphenylethyleneglycol sulphate content.** Life Sciences. 28(4):377-384, 1981.

The effects of acutely and chronically administered antidepressants on the clonidine induced decrease in rat brain 3-methoxy-4-hydroxyphenylethyleneglycol sulphate (MHPG-SO4) content were investigated. Acutely administered mianserin increased rat brain MHPG-SO4 levels and prevented the clonidine induced reduction. The clonidine induced fall in MHPG-SO4 level was also absent following the acute administration of desipramine or nisoxetine. Chronic mianserin and nisoxetine increased MHPG-SO4 levels. Only chronic desopramine blocked the clonidine induced fall, the phenomenon developing between 5 and 9 days of chronic treatment. Results indicate that the ability of chronic desipramine to elicit subsensitivity of presynaptic alpha-adrenoceptors does not extend to the other four agents studied. 45 references. (Author abstract modified)

002909 Supavilai, Porntip; Karobath, Manfred. Karobath: Dept. of Biochemical Psychiatry, Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1090 Vienna, Austria **Action of pyrazolopyridines as modulators of (3H)flunitrazepam binding to the GABA/benzodiazepine receptor complex of the cerebellum.** European Journal of Pharmacology. 70(2):183-193, 1981.

The pyrazolopyridines etazolate and cartazolate directly stimulated 3H-flunitrazepam binding to male Sprague-Dawley rat cerebellar membranes by increasing the apparent affinity of 3H-flunitrazepam for its binding sites. The stimulation was dependent on the presence of chloride, bromide, iodide, nitrite, and nitrate, but not on fluoride, acetate, formate, or sulfate. The stimulation was inhibited by bicuculline methiodide and by chloride channel drugs such as picrotoxin. The pyrazolopyridines also indirectly affected benzodiazepine receptor binding by enhancing the apparent sensitivity of GABA recognition sites coupled to benzodiazepine binding sites: this sensitization was partially dependent on the presence of chloride ions. Results suggest that the pyrazolopyridines modulate 3H-flunitrazepam binding by acting at a site closely related to GABA receptor regulated chloride ion channels. 33 references. (Author abstract modified)

002910 Swann, Alan C.; Crawley, Jacqueline N.; Grant, Steven J.; Maas, James W. Yale University School of Medicine, Dept. of Psychiatry, 333 Cedar Street, New Haven, CT **Noradrenergic stimulation in vivo increases (Na, K)-adenosine triphosphatase activity.** Life Sciences. 28(3):251-256, 1981.

To evaluate the role of norepinephrine in regulating activity of (Na, K) adenosine triphosphatase in vivo, enzyme activity was measured in rat brain after electrical stimulation of the locus coeruleus and after administration of piperoxane. Both treatments resulted in increased (Na, K) adenosine triphosphatase activity in locus coeruleus projection areas, but not in corpus striatum. The increased activity was limited to the same side as the stimulating electrode. Destruction of noradrenergic fibers from the locus coeruleus with 6-hydroxydopamine prevented the increase in enzyme activity with piperoxane. 46 references. (Author abstract modified)

002911 Swann, Alan C.; Heninger, George R.; Roth, Robert H.; Maas, James W. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **Differential effects of short and long term lithium on tryptophan uptake and serotonergic function in cat brain.** Life Sciences. 28(4):347-354, 1981

The effects of short-term and longterm lithium treatment on tryptophan uptake and on tissue levels of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) were studied in 12 brain regions of the cat. Tryptophan uptake and 5-HIAA were significantly correlated in control cats. Short-term treatment caused parallel increases or decreases in tryptophan uptake and 5-HIAA. Long-term treatment consistently increased tryptophan uptake without corresponding changes in 5-HIAA. Relatively low cumulative doses of lithium may reduce the degreee to which tryptophan uptake is a limiting factor in the regulation of serotonin synthesis. 29 references. (Author abstract)

002912 Tallman, John F.; Mallorga, Pierre; Thomas, John W.; Gallager, Dorothy W. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Benzodiazepine binding sites: properties and modulation.** Advances in Biochemical Psychopharmacology. 26:9-18, 1981.

Recent investigations into the nature of changes in benzodiazepine binding elicited by pharmacological agents are reviewed, and the issues of multiple receptors are discussed. Studies indicate that GABA receptors and the central benzodiazepine binding closely interact in the membrane, and affinity changes may determine the ability of the system to function. Alterations in the number of benzodiazepine sites may also be of great importance in determining the magnitude of the GABA response or set point of response of the GABA system. Central benzodiazepine binding sites differ from peripheral sites and there may be several central sites. At least in the membrane, all of the central benzodiazepine binding sites may not be normally exposed. From the covalent labeling experiments with (3H)flunitrazepam and the simultaneous experiment with nonradioactive flunitrazepam, the binding sites for benzodiazepines, at least in the membrane, can probably interact with each other as well as with the GABA receptors. This may indicate a complex of several benzodiazepine sites together in the membrane with a GABA recognition unit and an ion channel. 48 references. (Author abstract modified)

002913 Tanaka, Shokichi; Tsujimoto, Akira. Dept. of Pharmacology, Hiroshima University, School of Dentistry, Hiroshima, Japan **Somatostatin facilitates the serotonin release from rat cerebral cortex, hippocampus, and hypothalamus slices.** Brain Research. 208(1):219-222, 1981.

The effect of somatostatin on the release of serotonin (5-HT) from the superfused slices of rat cerebral cortex, hippocampus, and hypothalamus preloaded with (3H)5-HT was examined. Somatostatin was found to facilitate dose dependently the electrically stimulated or high K stimulated release of (3H)5-HT. The order, from the greatest to least, of the stimulatory potency of somatostatin on the evoked release in the three areas of the brain was cortex, hippocampus, then hypothalamus. This report is the first direct evidence that somatostatin stimulates the release of serotonin, a putative transmitter in the CNS. 13 references. (Author abstract modified)

002914 Tang, Siu Wa; Seeman, Philip; Kwan, Sing. Psychopharmacology Unit, Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, Canada M5T 1R8 **Differential effect of chronic desipramine and amitriptyline treatment on rat brain adrenergic and serotonergic receptors.** Psychiatry Research. 4(2):129-138, 1981.

Serotonergic and adrenergic receptors were examined in rat brains by direct binding assays after chronic treatment with tricyclic antidepressants. Chronic amitriptyline (AMT) treatment (10mg/kg/day intraperitoneally for 21 days) decreased specific 3H-spiperone binding in the cortex and not in caudate nuclei. Specific 3H-dihydroalprenolol (3H-DHA) binding was reduced in cerebellar but not in cerebral cortex. Chronic desipramine (DMI) treatment given in the same dose schedule, on the other hand, decreased specific 3H-DHA binding in both cerebellar and cerebral cortex. Specific 3H-spiperone binding in the cerebral cortex was also reduced, but to a lesser extent than that in the AMT treated group. Scatchard analysis shows that reductions in 3H-spiperone or 3H-DHA binding in all cases were due to decreases in the number of binding sites (Bmax) and not to changes in dissociation constants (KD). No change was observed in 3H-serotonin, 3H-clonidine, or 3H-WB-4101 binding. The results show that there is no single common change in brain adrenergic and serotonergic receptors after chronic AMT and DMI treatment. 34 references. (Author abstract)

002915 Tenen, S. S.; Hirsch, James D. Dept. of Biological Research, G. D. Searle & Co., P.O. Box 5110, Chicago, IL 60680 **Beta-carboline-3-carboxylic acid ethyl ester antagonizes diazepam activity.** Nature. 288(5791):609-610, 1980.

The antagonism of diazepam activity by beta-carboline-3-carboxylic acid ethyl ester (beta-CEE) is described. The 50% protective dose of diazepam against pentylenetetrazole (PTZ) induced clonic seizures in mice was determined in mice pretreated with either normal saline or beta-CEE at 3.2, 10, or 32mg/kg. Pretreatment with beta-CEE produced a clear and pronounced dose responsive increase in the 50% protective dose of diazepam against PTZ induced clonic convulsions. In addition to confirming previous reports that beta-CEE is a potent displacer of 3H-diazepam, the data indicate that beta-CEE has activity that is opposite to, rather than similar to, that of diazepam. 13 references. (Author abstract modified)

002916 Thompson, Richard F.; Berger, Theodore W.; Berry, Stephen D. Department of Psychobiology, University of California, Irvine, CA 92717 **Brain mechanisms of learning.** In: Thompson, R., Neural mechansims of goal-directed behavior & learning. New York, Academic Press, 1980. 639 p. (p. 221-239).

In the classical conditioning of learning paradigm developed by Gormezano, the growth of the hippocampal unit response is shown to be completely predictive of subsequential behavioral learning. If the hippocampal response does not develop, the animal will not learn. If it develops rapidly, the animal will learn rapidly. If it develops slowly, the animal will learn slowly. The hippocampal response develops within the first few trials of training and is projected to other brain structures. The response appears to be generated primarily by pyramidal neurons. Finally, the temporal form of the hippocampal unit response predicts the temporal form of the behavioral response; it forms a temporal model of the learned behavioral response. In the context of goal-directed behavior, the hippocampus may function as a portion of the basic brain system that seems to code the goal-directed or salient aspects of the stimulus world in relation to adaptive behavior. 45 references.

002917 Tissot, R. Clinique psychiatrique de Geneve, CH-1225 Chene-Bourg, Switzerland /**Opiate receptors and sleep. II. Effects of microinjections of ethyl alcohol and pentobarbital in the median thalamus, periaqueductal gray matter and nucleus of the tractus solitarius of the rabbit.**/ Recepteurs de l'opium et sommeil: II. Effets de micro-injections d'alcool ethylique et de pentobarbital dans le thalamus median, la substance grise centrale periaqueducale et du noyau du tractus solitaire du lapin. Neuropsychobiology. 7(2):74-86, 1981.

The effects of microinjections of ethyl alcohol and pentobarbital in the median thalamus, periaqueductal gray matter, and nucleus of the tractus solitarius of the rabbit on EEGs and sleep were investigated. Like morphine, microinjections of optimal equimolar doses of ethyl alcohol and pentobarbital in the bulbo/mesencephalo/thalamic sleep inducing system of the rabbit produced sleep EEGs with abundant fast activity, which was blocked by naloxone. However, there is neither binding nor displacement by naloxone of ethyl alcohol or pentobarbital from the opiate receptor. It is speculated that ethyl alcohol and pentobarbital promote the release of endorphins or peptides which are specific ligands of all or some opiate receptors. 76 references. (Author abstract modified)

002918 Tollefson, Gary Dennis. University of Minnesota **A comparison of human muscarinic cholinergic receptor response to a number of psychotropics utilizing the radiolabeled antagonist, (3H)-quinuclidinyl benzilate. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2557-B, 1981. Ann Arbor, Univ. Microfilms No. 8102184, 97p., 1980.

The muscarinic cholinergic receptor in the human caudate was compared to that in the erythrocyte when subject to classical binding analysis and in the presence of a number of contemporary psychotropics (competitive displacement of specific binding). In both systems a specific, saturable, high affinitey site was described by saturation isotherm and in general agreement with other tissue sites. The differing affinities between the erythrocyte and caudate utilizing (3H)-quinuclidinyl benzilate (QNB) could imply two autonomous receptors or they may represent an identical receptor. Because of the strikingly similar relative affinities in both systems for a number of psychotropics, it would appear that the peripheral erythrocyte may offer an assessible parameter for the clinical study of central cholinopathic states. Results affirmed the considerable anticholinergic activity, as evidenced by competitive receptor affinity, for a number of contemporary psychotropics. Rank ordering indicates: dimethylated tricyclics are stronger anticholinergics than monomethylates in human tissue, both the tetracyclic antidepressant mianserin and the MAOI tranylcypromine are less competitive than the TCA's at the muscarinic receptor, and an inverse relationship between propensity to elicit extrapyramidal reactions (EPS) and displacement of high affinity binding sites exists. Explanations for agonist binding at a lower affinity than antagonist binding are offered. (Journal abstract modified)

002919 Torda, Tichomir; Yamaguchi, Isamu; Hirata, Fusao; Kopin, Irwin J.; Axelrod, Julius. Kopin: Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Mepacrine treatment prevents immobilization-induced desensitization of beta-adrenergic receptors in rat hypothalamus and brain stem.** Brain Research. 205(2):441-444, 1981.

Mepacrine treatment was found to prevent immobilization induced desensitization of beta-adrenergic receptors in rat hypothalamus and brainstem. Fewer beta-adrenoceptors were found in the hypothalamus and brainstem of rats subjected to repeated immobilization. Mepacrine treatment alone did not affect the number of beta-adrenergic receptors but prevented the stress induced decrease in beta-adrenoceptor density in the hypothalamus and brainstem. Mepacrine treatment resulted in a decrease in apparent Kd of the adrenoceptors in both areas of brain of unstressed, as well as stressed rats, whereas stress alone had no significant effect on affinity of the beta-receptors. Repeated immobilization stress increased alpha-2-adrenoceptors in the brainstem. 16 references.

002920 Tsujimoto, Akira; Tanaka, Shokichi. Dept. of Pharmacology, Hiroshima University School of Dentistry, Hiroshima, Japan **Stimulatory effect of somatostatin on norepinephrine release from rat brain cortex slices.** Life Sciences. 28(8):903-910, 1981.

The effect of somatostatin (SRIF) on norepinephrine (NE) release from brain tissue was determined on the superfused rat cerebral cortex slices preloaded with 3H-NE. SRIF was found to stimulate tritium (3H) overflow evoked electrically by 30% to 116%, although SRIF did not affect spontaneous 3H overflow. SRIF at concentrations which exhibited the stimulatory effect, barely inhibited the uptake of 3H-NE by cortex slices, while the reference drug, cocaine, markedly depressed the uptake. The stimulatory effect of SRIF was not reduced by phentolamine, an alpha-adrenoceptor blocker, which increased the evoked 3H overflow from the slices itself. These results suggest that SRIF does not produce its stimulatory effect by inhibiting the NE reuptake mechanisms or by interacting with the presynaptic alpha-adrenoceptors. Elevating Ca2 concentrations from 0.75mM to 2.25 mM in the superfusion fluid reduced the stimulatory effect of SRIF. It is possble that SRIF stimulates NE release by facilitating the availability of Ca2 for the release mechanisms. 24 references. (Author abstract modified)

002921 Turski, Lechoslaw; Turski, Waldemar; Czuczwar, Stanislaw J.; Kleinrok, Zdzislaw. Dept. of Pharmacology, Institute of Clinical Pathology, Medical School, Jaczewskiego 8, PL-20-090 Lublin, Poland **Effects of morphine and nalorphine on kainic acid-induced hypothermia in rats.** Psychopharmacology. 72(2):211-214, 1981.

The effects of morphine and nalorphine on kainic acid (KA) induced hypothermia in rats were investigated. Intraventricular administration of KA at the dose of 0.1mcg induced a significant depression followed rapidly by a slight elevation of rectal temperature. Morphine, which by itself elicits biphasic effect on the body temperature of rats (initially hypothermia followed by hyperthermia), slightly increased the KA induced hypothermia. Kainic acid did not cause any changes in the hyperthermic effect of low doses of morphine. Pretreatment of rats with nalorphine enhanced the kainic acid induced hypothermia. On the contrary, nalorphine reversed the hypothermic effect produced by morphine. Results suggest that morphine induced hypothermia and KA induced hypothermia are not mediated by the influence on the same type of receptors. 13 references. (Author abstract modified)

002922 Usdin, Ted B.; Creese, Ian; Snyder, Solomon H. Snyder: Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Regulation by cations of (3H)spiroperidol binding associated with dopamine receptors of rat brain.** Journal of Neurochemistry. 34(3):669-676, 1980.

Monovalent and divalent cations, as well as several chelating agents, increased the number of (3H)spiroperidol binding sites in rat corpus striata. Maganese was most potent, enhancing binding at a 1 mcM concentration; magnesium and calcium were at least two orders of magnitude less potent, and sodium, potassium, and lithium were still weaker. Divalent cations enhanced the potency of dopaminergic agonists in competing for (3H)spiroperidol binding, and this effect was independent of the ionic augmentation of (3H)spiroperidol binding. Divalent cations increased the association and dissociation rates of (3H)spiroperidol binding to dopamine receptor sites. 33 references. (Author abstract modified)

002923 van der Heyden, J. A. M.; Venema, K.; Korf, J. Dept. of Pharmacology, Philips Duphar B. V., C. J. van Houtenlaan 36, 1381 CP Weesp, The Netherlands **Biphasic and opposite effects of dopamine and apomorphine on endogenous GABA release in the rat substantia nigra.** Journal of Neurochemistry. 34(1):119-125, 1980.

A push/pull cannula technique was used to study the effects of dopamine (DA) and apomorphine on endogenous GABA release in the substantia nigra of Wistar rats. A 10mcM concentration of DA in the perfusion medium increased GABA release, whereas 50mcM DA decreased GABA release. Apomorphine at 10mcM decreased GABA release, but at 25mcM produced opposite effects. Haloperidol blocked the inhibitory effect of 25mcM DA and the excitatory effect of 100mcM apomorphine. Dibutyryl cyclic AMP and 2-amino-6,7-

dihydroxyl(1,2,3,4)tetrahydronapthalene inhibited nigral GABA release. Results suggest that dopaminergic processes in the substantia nigra affect GABA mediated neurotransmission. 65 references. (Author abstract modified)

002924 Van Loon, Glen R.; Appel, Nathan M. Dept. of Medicine, Medical Sciences Bldg., University of Toronto, Ontario M5S 1A8, Canada **Beta-endorphin-induced hyperglycemia is mediated by increased central sympathetic outflow to adrenal medulla.** Brain Research. 204(1):236-241, 1981.

The mediation of beta-endorphin induced hyperglycemia by increased central sympathetic outflow to adrenal medulla is described. Synthetic human beta-endorphin increased plasma glucose concentration when administered intracisternally in chronically cannulated, conscious, unrestrained, adult male rats. This hyperglycemic effect of beta-endorphin was blocked by prior systemic administration of naloxone, supporting mediation of the effect at opioid receptors in brain. Adrenal denervation blocked the beta-endorphin induced increase in plasma glucose, supporting a thesis that this effect is mediated at least in part by increased epinephrine secretion. The hyperglycemic response to intracerebral beta-endorphin was also blocked by either intracerebral hemicholinium 3 or somatostatin, supporting both a cholinergic link and a somatostatin neuron in the brain mechanisms regulating endorphin induced stimulation of sympathetic outflow. 23 references. (Author abstract modified)

002925 Voltattorni, Carla Borri; Minelli, Alba; Borri, Piero. Institute of Biological Chemistry, Faculty of Pharmacy, University of Perugia, I-06100 Perugia, Italy **The interaction of 2,3,4-trihydroxybenzylhydrazine with dopa decarboxylase from pig kidney.** Life Sciences. 28(1):103-108, 1981.

The interaction of 2,3,4-trihydroxybenzylhydrazine (Ro 4-5127) with dopa decarboxylase from pig kidney was investigated. The spectral modifications induced by addition of Ro 4-5127 to dopa decarboxylase indicate the binding of this compound to the coenzyme binding sites and allow the titration of the enzyme. Inhibition data indicate that Ro 4-5127 behaves as a pseudoirreversible inhibitory of dopa decarboxylase and that 100% inhibition is not reached at a 1:1 inhibitor/enzyme molar ratio, as expected from spectral data, but at a molar ratio of about 6.0. On this basis it would be possible to suggest, beside the coenzyme binding site, the existence on the enzyme molecule of other sites where the compound could bind without affecting its spectral feature. The interaction of Ro 4-5127 with dopa decarboxylase shows that in vivo Ro 4-5127 behaves as a more powerful inhibitor of dopa decarboxylase than its precursor trihydroxybenzylhydrazine seryl derivative (Ro 4-4602) indicating that the strong in vivo inhibition exerted by Ro 4-4602 might reflect the effective interaction of dopa decarboxylase with Ro 4-5127. 13 references. (Author abstract modified)

002926 Wagner, George C.; Schuster, Charles R.; Seiden, Lewis S. Dept. of Biopsychology, University of Chicago, Chicago, IL 60637 **Neurochemical consequences following administration of CNS stimulants to the neonatal rat.** Pharmacology Biochemistry and Behavior. 14(1):117-119, 1981.

Regional catecholamine levels were determined in the brains of Sprague-Dawley rats treated with methylamphetamine, d-amphetamine, or methylphenidate (12.5, 25, or 50mg/kg/day) from postnatal days 10 to 40. The higher doses of methylamphetamine and d-amphetamine induced long lasting depletions of dopamine in the caudate, but did not alter norepinephrine levels. Methylphenidate had no long-term effect on catecholamine levels. 20 references. (Author abstract modified)

002927 Wallis, Cleatus J.; Luttge, William G. Div. of Pharmacology, M-013, Dept. of Medicine, University of California, San Diego, La Jolla, CA 92093 **Influence of estrogen and progesterone on glutamic acid decarboxylase activity in discrete regions of rat brain.** Journal of Neurochemistry. 34(3):609-613, 1980.

In a study of the effect of steroids on glutamic acid decarboxylase (GAD) activity, ovariectomized Charles River rats were treated with 17beta-estradiol benzoate (1.0mcg/day) or progesterone (500mcg/day) for 3 days. Estradiol benzoate and progesterone were potent inhibitors of GAD activity in the arcuate nucleus, ventromedial hypothalamus, and corticomedial amygdala. Estrogen reduced the maximal velocity of GAD for glutamate as substrate. Combined treatment with estrogen (2 days) and progesterone (1 day) did not reduce GAD activity in ovariectomized animals except in the septum, indicating an interaction of the two hormones at the level of GAD. It is suggested that GAD activity is low under conditions that inhibit luteinizing hormone (LH) secretion, but comparatively high when LH secretion is stimulated. 32 references. (Author abstract modified)

002928 Wang, J.; Pollack, J.; Birnkrandt, D.; Demirian, L.; Gratton, I.; Pierson, R. N., Jr. Pierson: Div. of Nuclear Medicine, St. Luke's Hospital Center, Amsterdam Ave. at 114th St., New York, NY 10025 **Combined effects of alcohol and lithium on body composition in the rat model.** Pharmacology Biochemistry and Behavior. 14(1):41-47, 1981.

Alcohol markedly enhanced lithium (Li) retention in blood and muscle in Sprague-Dawley rats. The exchangeable sodium (Na) space was markedly enlarged by alcohol and Li, alone or in combination, as a result of extensive mobilization of bound bone Na and transfer to intracellular sites. Li was associated with a decreased food and fluid intake, and this effect was enhanced by alcohol. However, the decrease in intake did not result in nutritionally significant deficits; the observed abnormalities in body composition did not result from caloric, protein, potassium, Na, or calcium deficiencies. 27 references. (Author abstract modified)

002929 Williams, Jonathan H.; Azmitia, Efrain C. Azmita: Dept. of Anatomy, Mount Sinai School of Medicine, New York, NY 10029 **Hippocampal serotonin re-uptake and nocturnal locomotor activity after microinjections of 5,7-DHT in the fornix-fimbria.** Brain Research. 207(1):95-107, 1981.

The role of the hippocampal 5-hydroxytryptamine (5-HT) terminals in the control of locomotor activity was investigated by lesioning 5-HT axons in the fimbria with 5,7-dihydroxytryptamine (5,7-DHT). On the 14th to 21st nights after operation, nocturnal locomotor activity of rats was measured in photocell cages. Twenty eight to 30 days after operation, degeneration of 5-HT terminals was assessed by measuring in vitro (3H)5-HT reuptake in slices of dorsal hippocampus, ventral hippocampus, and the septum. For each rat, the levels of dorsal and ventral hippocampal (3H)5-HT reuptake were correlated negatively with the mean nocturnal activity from the seven nights of testing. Levels of dorsal, but not ventral, hippocampal (3H)5-HT reuptake were correlated negatively with the mean nightly decrement of activity. Results indicate that the increase in nocturnal locomotor activity caused by generalized depletion of 5-HT in the brain may be due to disruption of hippocampal 5-HT terminals supplied by the fornix fimbria. 22 references. (Author abstract modified)

002930 Willmore, L. James; Rubin, Jay J. Neurology Service (127) V.A. Medical Center, Gainesville, FL 32602 **Antiperoxidant pretreatment and iron-induced epileptiform discharges in the rat: EEG and histopathologic studies.** Neurology. 31(1):63-69, 1981.

The EEG and histopathologic patterns in animals with recurrent epileptiform discharges induced by intracerebral injection of iron were investigated in Ss receiving and not receiving the antiperoxidants, alpha-tocopherol and selenium. Following injection of aqueous solution of iron salts, the principal metallic ion of whole blood, into rat isocortex, serial EEGs showed that 94% of untreated animals developed epileptiform discharges. Pretreatment with alpha-tocopherol and selenium prevented development of iron induced epileptiform activity in 72% of animals. Histopathologic assessment of serial sections stained with Nissl, hematoxylin, and eosin, and prussian blue showed cavitation, neuronal pyknosis and loss, and astrogliosis in untreated animals. The site of iron injection in animals treated with antiperoxidants contained only an area of neuronal pyknosis. The efficacy of antioxidants in preventing development of iron induced cavitation, gliosis, and epileptiform discharges suggests that peroxidative injury may be important in the development of experimental epilepsy induced by isocortical injection of ferrous chloride. 67 references. (Author abstract modified)

002931 Willner, Paul; Montgomery, Tony. Psychology Dept., City of London Polytechnic, Old Castle St., London E1, England **Neurotransmitters and depression: too much, too little, too unstable -- or not unstable enough?** Trends in NeuroSciences. 3(8):201, 1980.

The modulation of amphetamine induced anorexia in rats by the tricyclic antidepressants desmethylimiprimine (DMI) and iprindole was investigated in relation to the issue of whether the net effect of antidepressants is a decrease or an increase in brain noradrenaline (NA). Results suggest that during withdrawal from DMI or iprindole, NA transmission is decreased. However, during drug treatment this effect is exactly offset by the acute, potentiating effects of the drugs. It is concluded that following an initial increase, tricyclic antidepressants return the efficacy of the NA synapse to its status quo ante, with no net increase or decrease. This suggests that the problem in depression is neither too much NA, nor too little. 14 references.

002932 Wolfe, Barry B.; Augustyn, Damian H.; Majocha, Ronald E.; Dibner, Mark D.; Molinoff, Perry B.; Baldessarini, Ross J.; Walton, Kenneth G. Walton: Dept. of Biology, Maharishi International University, Fairfield, IA 52556 **Effects of isoproterenol on the development of beta-adrenergic receptors in brain cell aggregates.** Brain Research. 207(1):174-177, 1981.

The development of binding sites for the beta-adrenergic receptor antagonist (125I)iodohydroxybenzylpindolol in reaggregate cultures of fetal rat brain was investigated. Beta-adrenergic receptor density increased rapidly between 6 and 22 days in culture at which time maximal density was attained. When cultures were grown in the presence of the beta-adrenergic receptor agonist isoproterenol, the development of receptors was inhibited markedly. Cultures also were grown for 15 days in the presence of isoproterenol and then for 7 to 14 days in the absence of isoproterenol. Following the removal of the agonist, binding sites developed, but to only approximately 50% of the density seen in control cultures. 22 references. (Author abstract)

002933 Wu, P. H.; Phillis, J. W.; Bender, A. S. Phillis: Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Do benzodiazepines bind at adenosine uptake sites in CNS?** Life Sciences. 28(9):1023-1031, 1981.

A series of known adenosine uptake inhibitors were tested for their ability to inhibit diazepam binding to synaptosomal membranes, and the relationship between diazepam binding sites and adenosine uptake sites was assessed. It is noted that agents which possess benzodiazepine like activities such as CL218,872, zopiclone, and fominoben, and which displace benzodiazepine binding to brain cell membranes are also inhibitors of adenosine uptake into brain synaptosomes. Adenosine uptake inhibitors (dipyridamole, hexobendine, papaverine, 6-(2-hydroxy-5-nitrobenzyl) thioguanosine) which competitively inhibit adenosine uptake, presumably by blocking adenosine binding to its carrier protein, are competitive inhibitors of diazepam binding to the brain membrane receptors. The finding of a pronounced correlation between inhibition of benzodiazepine binding and inhibition of adenosine uptake further supports the proposal that benzodiazepines may exert part of their pharmacological action through the inhibition of adenosine uptake. 42 references. (Author abstract modified)

002934 Wurtman, Richard J.; Magil, Shelia G.; Reinstein, Daniel K. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139 **Piracetam diminishes hippocampal acetylcholine levels in rats.** Life Sciences. 28(10):1091-1093, 1981.

The effect of piracetam on hippocampal acetylcholine (ACh) levels in rats was investigated. Based on previous studies, septohippocampal cholinergic neurons were thought to be involved in certain components of memory. Piracetam administration caused a significant reduction in hippocampal ACh among naive animals, without significantly modifying choline levels. In the dosage range tested (30mg/kg to 300mg/kg) no clear dose/effect relationship was noted. It is speculated that if piracetam actually facilitates hippocampal cholinergic neurotransmission, and if this neurochemical effect is related to its reported action on memory, then it might be possible to amplify its utility by coadministration of piracetam and choline or lecithin. 19 references.

002935 Wuster, Michael; Schulz, Rudiger. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munchen 40, West Germany **Differential effects of potassium on the potency of different opioids in the mouse vas deferens.** Naunyn-Schmiedeberg's Archives of Pharmacology. 315(2):181-184, 1980.

The effects of potassium on the ability of various opioids to inhibit electrically evoked twitches in the NMRI mouse vas deferens were determined. In general, opioid potency decreased as the concentration of potassium increased. Mu-receptor and delta-receptor agonists were the least sensitive to the effects of potassium; the concentration required to cause half maximal inhibition increased only twofold at 15mM potassium. At this concentration, the dynorphin receptor and kappa-receptor agonists showed up to an eightfold loss of potency and dynorphin1-13 showed a fivefold loss of inhibitory activity. Results suggest that potassium may have a modulatory action on dynorphin receptors and kappa-receptors. 20 references. (Author abstract modified)

002936 Yamamoto, Minoru; Tachikawa, Shiro; Maeno, Hiroo. Central Research Laboratories, Yamanouchi Pharmaceutical Co., Ltd. Azusawa, Itabashi-ku, Tokyo 174, Japan **Evoked potential studies of porcine calcitonin in rabbits.** Neuropharmacology. 20(1):83-86, 1981.

The effects of porcine calcitonin on evoked potentials of rabbits to painful stimuli were examined. The development of the long latency cortical potentials evoked by electrical stimulation of both the tooth pulp and sciatic nerve in gallamine immobilized rabbits was inhibited by intracerebroventricular calcitonin (17U/kg) but not the intravenous injection of 50U/kg. Pretreatment with naloxone showed no influence upon the inhibitory effect of calcitonin, though it completely antagonized the effect of morphine. The results suggest the analgesic effect of intracerebroventricular porcine calcitonin can be attributed to blocking of pain pathways in the CNS in a manner distinct from the narcotic analgesic. 11 references. (Author abstract)

002937 Yohe, Herbert C.; Ueno, Kunihiro; Chang, Nan-Chen; Glaser, Gilbert H.; Yu, Robert K. Yu: Dept. of Neurology, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **Incorporation of N-acetylmannosamine into rat brain subcellular gangliosides: effect of pentylenetetrazol-induced convulsions in brain gangliosides.** Journal of Neurochemistry. 34(3):560-568, 1980.

The radioactive labeling of total ganglioside fractions and of major individual gangliosides in 20-day-old male rat brain microsomes and synaptosomes was studied after intracerebral injection of the sialic acid precursor, N-acetylmannosamine. After this labeling pattern was established, the effect of pentylenetetrazol on brain gangliosides was examined in detail. Significant decreases in radioactive label were seen in the polysialogangliosides GT1b and GQ1b from the synaptosomal and microsomal fractions of the convulsed animals. The decreases may have been due to the activation of membrane bound neuraminidase present with gangliosides in neuronal tissue. 40 references. (Author abstract modified)

002938 Young, W. Scott, III; Kuhar, Michael J. Kuhar: Dept. of Psychiatry and the Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Neurotensin receptor localization by light microscopic autoradiography in rat brain.** Brain Research. 206(2):273-285, 1981.

Light microscopic localization of the neurotensin receptor in slide mounted tissue sections using autoradiographic localization of (3H)neurotensin binding sites is described. Large variations in receptor distribution were found, even in small areas. In many regions, the distribution of the receptor paralleled that of the immunoreactive neurotensin found in other studies. Results suggest sites of neurotensin's action in producing various physiological effects such as hypothermia and analgesia. 28 references. (Author abstract modified)

002939 Zaczek, R.; Nelson, M.; Coyle, J. T. Dept. of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Kainic acid neurotoxicity and seizures.** Neuropharmacology. 20(2):183-189, 1981.

The effects of pretreatment with anesthetics and anticonvulsants on the neurotoxic action of kainic acid injections in the male Sprague-Dawley rat hippocampus and striatum were examined. Brief anesthesia with ether did not block the seizures as severe degeneration of the hippocampal CA1-4 pyramids and granule cells induced by kainic acid. Prolonged anesthesia with chloral hydrate/pentobarbital or gamma-butyrolactone protected most hippocampal neurons and blocked seizures. Phenobarbital (100mg/kg) prevented cortical seizures but provided minimal protection against hippocampal neuronal degeneration. Prolonged anesthesia with chloral hydrate/pentobarbital also attenuated the neurotoxic effects of kainic acid in the striatum. It is concluded that the anesthetic properties of drugs, rather than their anticonvulsant action, protected against the neurotoxic effects of kainic acid at the site of the injection. 28 references. (Author abstract modified)

002940 Zakharov, N. D.; Kravtsov, A. N.; Orlov, I. V. Institut normal'noy fiziologii im. P. K. Anokhina AMN SSSR, Moskva, USSR **/Action of cyclic 3',5'-adenosine monophosphate on central neurons./** O deystvii tsiklicheskogo 3',5'-adenozinmonofosfata na tsentral'nyye neyrony. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 30(6):1279-1283, 1980.

Action of cyclic 3',5'-adenosine monophosphate (cAMPh) on central neurons was studied in nonanesthetized and nonimmobilized rabbits. Neocortical nerve elements were identified according to their responses to stimulation of the fibers of the pyramidal tract. Unit responses in the cortex and thalamus to the cAMPh were examined by means of microiontophoresis. The impulse activity of the neurons was recorded through the central channel of multichannel glass microelectrodes, filled with a solution of NaCl. Results show that cAMPh changes the pattern of background unit activity, increasing or decreasing the discharge frequency; cAMPh changes unit responses both to acetylcholine and noradrenaline, and participates both in adrenergic and acetylcholinergic mechanisms of excitation processing in brain neurons. 23 references. (Journal abstract modified)

002941 Zhadina, S. D.; Vinogradova, O. S.; Bragin, A. G. Instituta biologicheskoy fiziki Akademii nauk SSSR, Pushchino-na-Oke, USSR **/The effects of acetylcholine and glutamate on septal neurons in vitro./** Vliyaniye atsetilkholina i glyutamata na neyrony septum in vitro. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 30(2):392-397, 1980.

The effects of acetylcholine and glutamate on neurons of the medial septal nucleus were studied in slices of the guinea-pig brain in vitro. Glutamate produced a stereotypic initial activating effect, but in many units (12 out of 31) the activating phase was followed by a decrease of discharge frequency and an increase in spike amplitude. The effects of acetylcholine depended upon the type of spontaneous neuronal activity. In units with a regular pacemaker like activity, it produced an increase of discharge frequency with slow, gradual onset and offset of response. In neurons with an irregular burst activity, the application of acetylcholine evoked rhythmic bursts or increased their regularity with variable changes of the mean frequency in different units. Results show two functional types of units in the medial septum. 23 references. (Journal abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

002942 Adams, P. M.; Beauchamp, R.; Alston, C. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX 77550 **Potentiation of apomorphine and d-amphetamine effects by naloxone.** Life Sciences. 28(6):629-634, 1981.

The effects of naloxone, an opiate antagonist, on the stereotypic behavior and locomotor activity induced by apomorphine and d-amphetamine were studied. Groups of adult male Sprague-Dawley rats were first tested for stereotypy and locomotor activity after apomorphine or d-amphetamine. Groups were subsequently tested with saline or naloxone plus the previously used dosage of apomorphine or d-amphetamine. Naloxone alone did not produce stereotypy, but did significantly reduce locomotor activity. Naloxone potentiated apomorphine and d-amphetamine induced stereotypy. Apomorphine induced activity was increased by naloxone, but d-amphetamine induced activity at 2.5mg/kg was reduced. Results are compatible with the suggestion that naloxone may potentiate both apomorphine and d-amphetamine by inhibiting an opiate receptor mechanism which normally interacts with catecholamine neuronal action. 13 references. (Author abstract)

002943 Advokat, Claire. Dept. of Pharmacology, University of Illinois College of Medicine, P.O. Box 6998, Chicago, IL 60680 **Analgesic tolerance produced by morphine pellets is facilitated by analgesic testing.** Pharmacology Biochemistry and Behavior. 14(2):133-137, 1981.

Analgesic tolerance induced by morphine pellets was examined in rats using the nociceptive tail flick reflex. Analgesic responses of animals who received preliminary tail flick tests after morphine implantation were significantly lower than responses of naive, nontested animals. Previously tested animals were also significantly more tolerant to a morphine challenge than nontested animals. A dose response curve to morphine was not obtained, at the doses used here, from previously tested animals, whereas naive animals responded to morphine in a dose dependent manner. Environmental modulation of the tail flick reflex represents an elementary form of behavioral plasticity which may prove useful for neural analyses of simple reflex systems. 15 references. (Author abstract)

002944 Advokat, Claire. Dept. of Pharmacology, University of Illinois at the Medical Center, P.O. Box 6998, Chicago, IL 60680 **Environmental modulation of analgesic tolerance induced by morphine pellets.** Pharmacology Biochemistry and Behavior. 14(2):139-142, 1981.

The development of analgesic tolerance to the nociceptive tail flick test was examined in morphine implanted rats. Animals repeatedly exposed to a nonfunctional tail flick apparatus after implantation, were significantly more tolerant than nonexposed animals, on subsequent tests with the functional apparatus. In contrast, prior exposure to an alternate nociceptive, hotplate test, did not significantly modify tolerance on the tail flick. Facilitation of tolerance, produced by prior tail flick assessment, was maintained for at least 1 week following the last test, but only if the morphine pellet was not removed. If the pellet was removed, the influence of prior analgesic assessment was not retained. The substantial plasticity exhibited by the spinal tail flick reflex suggests the utility of this response for investigations of neural correlates of behavior. 9 references. (Author abstract)

002945 Albert, D. J. Psychology Dept., University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Cholinergic, dopaminergic, noradrenergic, or glutaminergic stimulation ventral to the anterior septum does not specifically suppress defensive behavior.** Pharmacology Biochemistry and Behavior. 14(1):35-39, 1981.

Defensive behavior in male hooded rats was suppressed by intracranial infusion of carbachol or physostigmine, but not by a mixture of carbachol and atropine sulfate or by dopamine, norepineprhine, or glutamate. The cholinergic antagonists atropine methyl nitrate and atropine sulfate did not increase reactivity when infused ventral to the anterior septum, but the nonspecific blocking agent lidocaine was effective. Infusion of carbachol ventral to the anterior septum suppressed eating and general activity as well as defensiveness, suggesting the effect was nonspecific. It is concluded that the specific modulation of defensiveness by the neural system ventral to the anterior septum is not mediated by acetylcholine, dopamine, norepinephrine, or glutamate. 34 references. (Author abstract modified)

002946 Albertson, T. E.; Peterson, S. L.; Stark, L. G.; Baselt, R. C. Dept. of Internal Medicine, School of Medicine, University of California, Davis, CA 95616 **Valproic acid serum levels and protection against kindled amygdaloid seizures in the rat.** Neuropharmacology. 20(1):95-97, 1981.

The anticonvulsant effectiveness of valproic acid (VPA) against amygdaloid seizures was studied in a systematic, multiple dose evaluation in rats. VPA produced a significant decrease in afterdischarge length and seizure rank scores at 200mg/kg. No obvious neurological deficits were noted at this dose. At 30 min postinjection, the degree of seizure protection and increased serum levels of VPA were significantly correlated. Also at 30 min postinjection, the ED50 was found to be 200mg/kg and the ESL50 was estimated to be 500mg/L. 16 references. (Author abstract modified)

002947 Altshuler, Harold L.; Applebaum, Eve; Shippenberg, Toni S. Neuropsychopharmacology Research Section, Texas Research Institute of Mental Sciences, Houston, TX 77030 **The effects of opiate antagonists on the discriminative stimulus properties of ethanol.** Pharmacology Biochemistry and Behavior. 14(1):97-100, 1981.

Naloxone (1.0 and 10.0mg/kg) and naltrexone (1.0 and 10.0mg/kg) were injected intramuscularly in male Sprague-Dawley rats trained to discriminate ethanol from saline. Neither opiate antagonist significantly altered ethanol discrimination performance. Results indicate that the discriminative stimulus properties of ethanol are not dependent on intact opiate pathways. The discriminative stimulus property of ethanol is probably mediated by a different mechanism than its reinforcing effect, which appears to be mediated by endogenous opiate systems. 32 references. (Author abstract modified)

002948 Arnt, Jorn; Christensen, Anne Vibeke. Dept. of Pharmacology and Toxicology, H. Lundbeck and Co. A/S, Ottiliavej 7-9, UK-2500 Valby, Denmark **Differential reversal by scopolamine and THIP of the antistereotypic and cataleptic effects of neuroleptics.** European Journal of Pharmacology. 69(1):107-111, 1981.

Scopolamine reversed neuroleptic induced catalepsy and neuroleptic blockade of amphetamine induced stereotypies in male Wistar rats. Butyrophenones were sensitive to scopolamine reversal, but the thioxanthenes cis-Z-flupentixol and piflutixol were not. The GABA agonist 4,5,6,7-tetrahydroisoxazolo(5,4-C)pyridin-3-ol did not alter the effects of cis-Z-flupentixol, fluphenazine, or haloperidol. The relevance of these findings to the use of stereotypy and catalepsy tests to screen for antischizophrenic effects and extrapyramidal side-effects is discussed. 10 references. (Author abstract modified)

002949 Ashmarin, I. P.; Antonova, L. V.; Titov, S. A.; Maksimova, L. A.; Kamenskiy, A. A. Kafedra biokhimii MGU im. M. V. Lomonosova, Moskva, USSR **/Possible mechanisms of effect of ACTH4-10 and its analog, containing D-isomer of phenylalanine, on behavior./** Vozmozhnyye mekhanizmy raznonapravlennogo deystviya AKTG4-10 i yego analoga, soderzhashchego D-izomer fenilalanina, na povedeniye. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 30(6):1196-1203, 1980.

Possible mechanisms of effect of ACTG4-10 and its analog, containing D-isomer of phenylalanine, on behavior was studied in male white rats. The effect of these two oligopeptides, namely ACTG4-10 and hexopeptide met-glu-his-D-phen-lis-L-phen (Dphen-GP) on memorizing the situation and on the orienting and investigating reaction was examined using the method of elaboration of the food procuring habit in a T-maze and by the open-field method. Results show that these peptides in a dose of 15mcg/kg with certain periods of administration, have an opposite effect on maze learning but a similar effect on memory in the open field. ACTG4-10 slightly increased motor activity in the open field, whereas Dphen-GP decreased it considerably. These results suggest that ACTG4-10 improves the formation of trace processes independently of the sign of reinforcement, whereas Dphen-GP selectively enhances defensive reaction and memorization connected with negative reinforcement. 13 references. (Journal abstract modified)

002950 Astrachan, David I.; Davis, Michael. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Spinal modulation of the acoustic startle response: the role of norepinephrine, serotonin and dopamine.** Brain Research. 206(1):223-228, 1981.

The roles of norepinephrine (NE), serotonin (5-HT), and dopamine (DA) in spinal modulation of the acoustic startle response were investigated in rats. The postdrug infusion startle responses for each rat were compared with their respective predrug baseline to determine change in startle amplitude following administration of 5-HT (with and without pargyline pretreatment), 5-methoxy-N,N-dimethyltryptamine (5-MeODMT), NE, phenylephrine, isoproterenol, DA, or apomorphine. In contrast to 5-HT and NE, neither DA nor the DA agonist apomorphine increased acoustic startle when given intrathecally. Results suggest the possibility that a variety of drug or environmental manipulations that increase startle (e.g., sensitization to background noise, potentiation due to prior condition) might be expressed by release of 5-HT and/or NE into the spinal cord. Results also demonstrate the importance of the spinal cord as a potential target mediating drug effects on behavior. 21 references.

002951 Atterwill, C. K. MRC Developmental Biology Unit, Institute of Neurology, 33 John's Mews, London WC1, England **Effect of acute and chronic tri-iodothyronine (T3) administration to rats on central 5-HT and dopamine-mediated behavioural responses and related brain biochemistry.** Neuropharmacology. 20(2):131-144, 1981.

Tri-iodothyronine (T3) produced complex changes in central dopamine (DA) and 5-hydroxytryptamine (5-HT) systems in male Sprague-Dawley rats. Acute or chronic T3 treatment enhanced the hyperactivity response to tranylcypromine (TCP) plus L-DOPA. Behavioral responses to apomorphine were attenuated and the cataleptic response to haloperidol was potentiated in rats treated chronically with T3, but not in acutely treated animals. Striatal 3H-spiroperidol binding was not altered in chronically treated animals. The hyperactivity response to quipazine, 5-methoxy-N,N-dimethyltryptamine, or TCP plus L-tryptophan (TP) was markedly enhanced by chronic or acute T3 treatment. The accumulation of 5-HT and TP after TP injection was not altered by chronic T3. 51 references. (Author abstract modified)

002952 Avery, D. D.; Hawkins, M. F.; Wunder, B. A. Dept. of Psychology, Colorado State University, Fort Collins, CO 80523 **The effects of injections of bombesin into the cerebral ventricles on behavioral thermoregulation.** Neuropharmacology. 20(1):23-27, 1981.

The effects of injections of bombesin into the cerebral ventricles on behavioral thermoregulation were investigated. Data are reported here which indicate that bombesin also alters thermoregulation at ambient temperatures at, or above, thermoneutrality. Bombesin was microinjected into the lateral ventricles of unrestrained rats trained to press a bar to escape radiant heat and receive a draft of 23 degrees C plus or minus 1 degree C room air. Control injections did not alter the bar-press response and rectal temperature rose an average of 2.4 degrees C during the 30 min testing session. Following bombesin injections, however, the number of bar presses increased and body temperature did not rise above euthermic values. Additionally, animals which received bobesin were monitored at room temperature when they were removed from the apparatus after behavioral testing. These animals became hypothermic. Results are discussed in relation to the setpoint of body temperature. 11 references. (Author abstract modified)

002953 Barrett, R. J.; Leith, Nancy J. V. A. Medical Center, Nashville, TN 37203 **Tolerance to the discriminative stimulus properties of d-amphetamine.** Neuropharmacology. 20(3):251-255, 1981.

Male F-344 rats responding for milk on a variable interval 20 sec schedule of reinforcement were trained to discriminate d-amphetamine (0.5, 1.0, or 1.3mg/kg) from saline. Two days after chronic amphetamine treatment (78mg/kg over 4 days), rats were tested for tolerance at a dose that normally produced about 80% drug lever responding. Rats in all three groups showed tolerance to the cue properties of amphetamine, and tolerance was complete in the two lower dose groups. 21 references. (Author abstract modified)

002954 Bedford, John A.; Nail, Greg L.; Borne, Ronald F.; Wilson, Marvin C. Research Institute of Pharmaceutical Sciences, University of Mississippi, University, MS 38677 **Discriminative stimulus properties of cocaine, norcocaine, and N-allylnorcocaine.** Pharmacology Biochemistry and Behavior. 14(1):81-83, 1981.

Wistar rats trained to discriminate 5.0mg/kg cocaine from saline in a two bar operant chamber on a fixed-ratio 30 schedule of food reinforcement generalized from 2.5, 7.5, and 10mg/kg cocaine to the pretreatment cocaine and from 1.0mg/kg cocaine to saline. High doses of norcocaine (5.0 and 7.5mg/kg) generalized to cocaine, but 1.0mg/kg generalized to saline. A 20mg/kg dose of N-allylnorcocaine generalized to cocaine, but lower doses produced intermediate responding or generalized to saline. The data demonstrate that norcocaine and N-allylnorcocaine share similar stimulus properties with cocaine. Potency differences for these drugs are quite apparent and possible explanations for these are different lipid solubilities, rates of metabolism, dissociation constants and volumes of distribution. 13 references. (Author abstract modified)

002955 Benedek, G.; Obal, F., Jr.; Rubicsek, G.; Obal, F. Dept. of Physiology, University Medical School, Szeged, Hungary **Sleep elicited by olfactory tubercle stimulation and the effect of atropine.** Behavioural Brain Research. 2(1):23-32, 1981.

The effects of high frequency olfactory tubercle (TbOf) stimulations were studied on the EEG and behavior of freely moving cats. Results include: 1) TbOf stimulation elicited sleep similar in every respect to physiological sleep; 2) statistical evaluation of the results showed that primarily the appearance and maintenance of slow-wave sleep was facilitated by the stimulations. Stimulations during paradoxical sleep had no effect, but they did promote the recurrence of slow-wave sleep after the paradoxical sleep. The effect of stimulations during wakefulness depended on the ongoing activity; 3) TbOf stimulation brought about synchronization, which was characterized by a similar arousal threshold as for physiological sleep; and 4) atropine treatment prevented the behavioral effects and did not influence the EEG effects of the stimulations. 26 references. (Author abstract)

002956 Beninger, Richard J.; Phillips, Anthony G. Dept. of Psychology, Queen's University, Kingston, Ontario, K7L 3N6, England **The effects of pimozide during pairing on the transfer of classical conditioning to an operant discrimination.** Pharmacology Biochemistry and Behavior. 14(1):101-105, 1981.

Acquisition of an operant discrimination was enhanced in male Wistar rats previously exposed to pairings of the discriminative stimulus with food, compared to control animals. Rats that received the classical conditioning while under the influence of pimozide (1.0mg/kg) also showed enhanced acquisition of the discrimination when tested in an undrugged state. The role of dopaminergic neurons in the mechanism by which classical conditioning transfers to operant learning is discussed. 33 references. (Author abstract modified)

002957 Beyer, C.; Canchola, E.; Larsson, K. Secc. de Neuroendocrinologia, Subjefatura de Investig. Cientifica, Inst. Mexicano del Seguro Social, Apartado Postal 73-032, Mexico 73, D.F. **Fa-**

cilitation of lordosis behavior in the ovariectomized estrogen primed rat by dibutyryl cAMP. Physiology & Behavior. 26(2):249-251, 1981.

The effect of subcutaneous injections of dibutyryl cyclic AMP (0.5, 1, 2, 8, and 16mg) on the sexual behavior of ovariectomized, estrogen primed Wistar rats was studied. All but the lowest dose elicited lordosis in at least 50% of the rats. However, the response to dibutyryl cyclic AMP varied greatly among subjects, and no dose/response relationship was apparent. Theophylline (10mg) increased and prolonged the action of dibutyryl cyclic AMP. Bilateral injection of 50mcg dibutyryl cyclic AMP into the medial preoptic area of estrogen primed rats elicited lordosis in four of eight rats. Dibutyryl cyclic AMP did not produce sequential inhibition, which suggests its effect was not mediated by the secretion of adrenal progesterone. 14 references. (Author abstract modified)

002958 Borbely, Alexander A.; Neuhaus, Hans Ulrich; Tobler, Irene. Institute of Pharmacology, University of Zurich, CH-8006 Zurich, Switzerland **Effect of p-chlorophenylalanine and tryptophan on sleep, EEG and motor activity in the rat.** Behavioural Brain Research. 2(1):1-22, 1981.

The effects of a single injection of parachlorophenylalanine (PCPA) on sleep, motor activity and consummatory behavior were investigated in unrestrained rats which were continuously recorded with telemetric techniques on 2 control days and 6 drug days. Slow-wave sleep (SWS) was defined as the nonREM sleep fraction with a low predominant EEG frequency. In the 24 hour following PCPA administration, motor activity, and food intake were reduced and sleep was increased. SWS was massively enhanced, while REM sleep was depressed. The initial phase of sedation was followed by a phase of partial insomnia lasting 1 to 2 days. SWS and REMS were particularly depressed. Results indicate that depression of SWS and REMS, and the hyperactivity 1 to 2 days after PCPA administration, are a consequence of the reduced serotonin level, whereas the involvement of serotonergic mechanisms in the initial sedative phase and in the recovery phase is less clear. The existence of the daily distribution of sleep and activity, and of the specific pattern of SWS and REMS, indicates that the circadian sleep organization is little affected by serotonin depletion. 38 references. (Author abstract modified)

002959 Bowyer, J. F.; Winters, W. D. Dept. of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **The effects of various anesthetics on amygdaloid kindled seizures.** Neuropharmacology. 20(3):199-209, 1981.

The effects of the cataleptic anesthetics gamma-butyrolactone (GBL), phencyclidine (PCP), and ketamine (KET) and the depressant anesthetics pentobarbital (PB) and chloralhydrate (CH) on amygdaloid kindled seizures in male Sprague-Dawley rats were examined. Anesthetic doses of GBL and PCP had minimal effects on afterdischarge duration (AD) and behavioral ranking (BR) but were more inhibitory to the AD and BR than was pentylenetetrazol. PCP induced spontaneous seizure activity at anesthetic doses, and KET induced epileptoid activity at supranesthetic doses. KET, PB, and CH completely inhibited seizure activity at anesthetic doses. GBL did not block the kindling process. 24 references. (Author abstract modified)

002960 Bozarth, Michael A.; Wise, Roy A. Center for Research on Drug Dependence, Dept. of Psychology, Concordia University, Montreal, Quebec H3G 1M8, Canada **Intracranial self-administration of morphine into the ventral tegmental area in rats.** Life Sciences. 28(5):551-555, 1981.

The rewarding properties of morphine injected directly into the ventral tegmental area were investigated using a self-administration procedure. Experimentally naive rats demonstrated rapid acquisition of a lever-pressing response which produced a 100ng infusion of morphine sulfate solution. Response rates were relatively stable and markedly exceeded lever-press rates of rats passively receiving the same pattern of infusions (i.e. yoked control Ss). Intracranial self-administration was effectively blocked by naloxone, suggesting that this behavior is mediated through opiate receptors and is not the consequence of mechanical trauma, or changes in osmolarity or pH. 22 references. (Author abstract modified)

002961 Brady, Kathleen T.; Balster, Robert L. Balster: Pharmacology Dept., Medical College of Virginia, Virginia Commonwealth University, Box 613 MCV Station, Richmond, VA 23298 **Discriminative stimulus properties of phencyclidine and five analogues in the squirrel monkey.** Pharmacology Biochemistry and Behavior. 14(2):213-218, 1981.

The discriminative stimulus properties of phencyclidine (PCP) and five analogues were studied in the squirrel monkey. Ss were trained to discriminate PCP from saline in a two lever drug discrimination task on a fixed-ratio 32 schedule of food presentation. After reliable discriminative control of lever choice was established, dose response determinations for generalization to the training dose of PCP were made with several doses of PCP and its analogues. All drugs produced dose dependent PCP appropriate responding. In all cases, the dose necessary to suppress operant responding to 50% of vehicle rates was three to five times larger than the ED50 dose for drug lever appropriate responding. Results indicate marked similarities in the behavioral effects of these six arylcyclohexylamines. 29 references. (Author abstract modified)

002962 Brautigam, M.; Flosbach, C. W.; Herken, H. Herken: Pharmakologisches Institut der Freien Universitat Berlin, Thielallee 69/73, D-1000 Berlin 33, West Germany **Depression of reserpine-induced muscular rigidity in rats after administration of lisuride into the spinal subarachnoid space.** Naunyn-Schmiedeberg's Archives of Pharmacology. 315(2);177-179, 1980.

Muscular rigidity induced by reserpine (10mg/kg i.p.) in male Wistar rats was reduced by injections of lisuride hydrogen maleate into the lumbar spinal subarachnoid space and by i.p. injections of lisuride. Chronic catheterization of the lumbar spinal subarachnoid space permitted intrathecal drug administration in intact rats without anesthesia. Tonic activity of the gastrocnemius muscle was recorded electromyographically. The results suggest that the spinal cord is an important site of action of lisuride. 7 references. (Author abstract modified)

002963 Brown, David R.; Holtzman, Stephen G. Holtzman: Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Suppression of drinking by naloxone in the rat: a further characterization.** European Journal of Pharmacology. 69(3):331-340, 1981.

In male CFE rats deprived of water for 24 hours, naloxone (0.1 to 10mg/kg) produced a dose related suppression of drinking immediately after water presentation without altering latency to begin drinking. Naloxone also suppressed water consumption induced by isoproterenol and angiotensin-II. Naltrexone was more potent than naloxone in reducing isoproterenol induced water intake. Schedule induced polydipsia was not altered by naloxone or naltrexone. Results suggest that beta-endorphin is involved in the regulation of water intake and that narcotic antagonists attenuate regulatory but not adjunctive drinking. 30 references. (Author abstract modified)

002964 Buckett, W. Roger. Research Dept., Boots Co. Ltd., Nittingham NG2 3AA, England **Pharmacological studies on**

stimulation-produced analgesia in mice. European Journal of Pharmacology. 69(3):281-290, 1981.

Analgesia induced by peripheral caudal electrostimulation in CD1 female mice was not altered by drugs that affect catecholamine or GABA containing neurons. The stimulation induced analgesia was potentiated by serotonergic stimulation by 5-hydroxy-D,L-tryptophan and was reduced under some circumstances by serotonin depletion with p-chlorophenylalanine. The serotonin reuptake inhibitors fluoxetine and zimelidine had no effect. Stimulation induced analgesia was observed in mice tolerant to methadone and meperidine in adrenalectomized mice. 45 references. (Author abstract modified)

002965 Campbell, Byron A.; Raskin, Lisa A. Dept. of Psychology, Princeton University, Princeton, NJ 08544 **Canalization of arousal in the preweanling rat : effects of amphetamine on aggregation with surrogate stimuli.** Developmental Psychobiology. 14(2):127-137, 1981.

Preweanling rats, 15 days of age, were placed in an unfamiliar cage containing one of a variety of surrogate conspecific stimuli to study canalization of arousal and the effects of amphetamine on aggregation. Both furriness and temperature of the surrogate stimuli proved important determinants of conspecific aggregation (huddling). Preference for the soft, fluffy surrogate was not mediated by temperature conservation. Amphetamine restricted the range of surrogate stimuli that elicited huddling in the Ss. The findings that amphetamine produces a steeper generalization gradient of approach to surrogate stimuli further confirms a previous hypothesis that amphetamine canalizes arousal toward salient environmental stimuli. These findings have implicatons for the use of amphetamines to treat hyperkinetic children. 23 references. (Author abstract modified)

002966 Carter, C. J.; Pycock, C. J. Dept. of Neurology, Institute of Psychiatry, de Crespigny Park, Denmark Hill, London SE5, England **The role of 5-hydroxytryptamine in dopamine-dependent stereotyped behaviour.** Neuropharmacology. 20(3):261-265, 1981.

Large doses of 5-hydroxytryptamine (5-HT) receptor antagonists attenuated the stereotyped sniffing and biting induced by apomorphine in male Porton rats, but small doses of 5-HT antagonists converted sniffing to more intense biting. Small doses of 5-HT receptor stimulants converted sniffing to biting, but larger doses attenuated sniffing and biting. The complex role of 5-HT in the mediation of stereotyped behavior is discussed. It is suggested that the full spectrum of dopamine dependent stereotyped behavior in rats will not develop unless there is a concomitant increase in central 5-HT function. 31 references. (Author abstract modified)

002967 Chang, Yung-Feng; Hernandez, Manuel F.; Myslinski, Norbert R. Dept. of Biochemistry, University of Maryland Dental School, Baltimore, Md 21201 **Enhancement of hexobarbital-induced sleep by lysine and its metabolites.** Life Sciences. 28(4):407-413, 1981.

The enhancement of hexobarbital induced sleep by lysine and its metabolites was investigated. Lysine was shown to be metabolized in the rat brain to pipecolic acid, which is a precursor of piperidine. Lysine and its time for their effect on the sleeping time induced by hexobartial in the rat. Only L-lysine and D-lysine were found to prolong sleeping time significantly without toxic effect. A 3 day pretreatment with L-lysine produced an even more profound sleep prolongation. In most cases sleep enhancement was accompanied by a significant shortening of the time of sleep onset. Quantification of brain hexobarbital levels in the control and treated rats indicates that prolongation of sleeping time was not produced by inhibition of hexobarbital metabolism. The sleep prolonging effect of lysine, therefore, may be a direct action of lysine, or the metabolite(s) derived in vivo from lysine, on the CNS. 39 references. (Author abstract modified)

002968 Chiodo, Louis A.; Caggiula, Anthony R.; Saller, Charles F. Psychobiology Program, University of Pittsburgh, Pittsburgh, PA 15260 **Estrogen potentiates the stereotypy induced by dopamine agonists in the rat.** Life Sciences. 28(7):827-835, 1981.

Repeated weekly treatment with 100mcg/kg of estradiol benzoate (EB) to ovariectomized female rats was found to intensify the stereotypy induced by the dopamine agonists amphetamine and apomorphine. A similar effect on amphetamine stereotypy was produced 48 hours after a single injection of 10mcg/kg of EB. The fact that EB failed to increase blood or brain levels of either 3H-amphetamine or 3H-apomorphine suggests that these behavioral effects were not due to altered peripheral drug metabolism or uptake into the brain. The enhancement of stereotypy produced by EB is viewed as one manifestation of a more complex modulatory influence of estrogen on DA function. 26 references. (Author abstract)

002969 Colotla, Victor A.; Bautista, Samuel; Torres-Chazaro, Octavio. Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico **/Brief communication: behavioral recovery after toluene exposure in rats./** Communicion breve: recuperacion conductual despues de exposicion al tolueno en ratas. Revista Mexicana de Analisis de la Conducta. 6(1):103-111, 1980.

Behavioral recovery after toluene exposure was measured in five albino rats. The results show that during the recovery sessions (after toluene dosage) the differential reinforcement of low rate performance decreased to baseline levels, but the fixed-ratio performance remained at low levels. During the time out periods, the increase in the number of responses which occurred during exposure to the solvent decreased to baseline in the postdose session. The response rate in the postdose session increased progressively. These results can be explained by the fact that the concentration of toluene in the blood grows progressively with time and is related to the deterioration of behavior. 10 references. (Journal abstract modified)

002970 Concannon, James T.; Schechter, Martin D. Dept. of Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Hyperactivity in developing rats: sex differences in 6-hydroxydopamine and amphetamine effects.** Pharmacology Biochemistry and Behavior. 14(1):5-10, 1981.

Possible sex differences in activity and response to d-amphetamine were studied in Sprague-Dawley rats given intracisternal injections of 6-hydroxydopamine (6-OHDA) or its vehicle at 5 days of age. Males treated with 6-OHDA were hyperactive at 27 days of age, but treated females were hypoactive relative to the vehicle treated controls. The stimulant effect of d-amphetamine on activity was attenuated in 6-OHDA treated males and enhanced in treated females, compared to controls. No conclusive evidence was found for the ability of d-amphetamine to decrease 6-OHDA induced hyperactivity, however the results implicate the role of sex as subjects in modulating the effects of 6-OHDA and d-amphetamine on activity in developing rats. 24 references. (Author abstract modified)

002971 Cowen, P. J.; Green, A. R.; Nutt, D. J.; Martin, I. L. MRC Clinical Pharmacology Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Ethyl beta-carboline carboxylate lowers seizure threshold and antagonizes flurazepam-induced sedation in rats.** Nature. 290(5801):54-55, 1981.

The hypothesized anticonvulsant, hypnotic, and anxiolytic actions of ethyl beta-carboline-3-carboxylate (beta-CCE) were investigated in rats. In contrast to the benzodiazepines, beta-CCE lowered seizure threshold and reversed the sedative effect of flurazepam. It is suggested that if beta-CCE has a close structural relationship to the endogenous ligand, benzodiazepines may be antagonistic at the receptor site. It is concluded that beta-CCE has effects opposed to the benzodiazepines, but not that the reversal of the flurazepam induced sedation and the convulsant effects of beta-CCE are mediated through the same subpopulation of benzodiazepine receptors. 19 references. (Author abstract modified)

002972 Crawley, Jacqueline N.; Marangos, Paul J.; Paul, Steven M.; Skolnick, Phil; Goodwin, Frederick K. Clinical Psychology Branch, National Institute of Mental Health, Bethesda, MD 20205 **Interaction between purine and benzodiazepine: inosine reverses diazepam-induced stimulation of mouse exploratory behavior.** Science. 211(4483):725-727, 1981.

The behavioral effects of benzodiazepines in mice were investigated. Inosine, 2-deoxyinosine, and 2-deoxyguanosine completely reversed the increase in exploratory activity elicited in mice by diazepam. The inhibition of exploratory behavior by purines occurred at doses that when given alone have no effect on exploratory behavior. 7-Methylinosine, which does not bind to the brain benzodiazepine binding site in vitro, had no effect on the diazepam induced increase in exploratory behavior. Behavioral effects produced by various combinations of inosine and diazepam indicate that the interaction between purine and benzodiazepine is antagonistic and support the hypothesis that the naturally occurring purines function in anxiety related behaviors that respond to benzodiazepine treatment. 21 references. (Author abstract)

002973 Cuomo, V.; Cortese, I.; Racagni, G. Institute of Pharmacology, University of Bari, Bari, Italy **Effects of morphine and chlordiazepoxide on avoidance behaviour in two inbred strains of mice.** Neuropharmacology. 20(3):301-304, 1981.

The effects of morphine and chlordiazepoxide on shuttlebox avoidance behavior in male DBA/2J (DBA) and C57BL/6J (C57) mice were studied. The DBA mice reached higher avoidance levels than did the C57 mice after saline administration. Morphine facilitated avoidance responding in C57 mice but not in DBA mice. Improved avoidance behavior was seen in both strains after chlordiazepoxide administration. A subthreshold dose of chlordiazepoxide enhanced the effect of morphine on avoidance behavior in DBA mice, but no interaction between the two drugs was seen in C57 mice. 10 references. (Author abstract modified)

002974 Davis, Stephen F.; Whiteside, David A.; Dickson, Virginia A. Thomas, Roger L.; Heck, Douglas G. Emporia State University, Emporia, KS 66801 **Conditioning and retention of defensive burying as a function of Elavil and Thorazine injection.** Bulletin of the Psychonomic Society. 17(2):107-110, 1981.

The effects of amitriptyline (Elavil) and chlorpromaxine (Thorazine) on conditioning and retention of defensive burying were investigated. Three groups of rats received i.p. injections of Thorazine, Elavil, and isotonic saline, respectively, prior to defensive burying testing. During the initial testing session, Thorazine injected Ss spent significantly less time engaged in defensive burying and accumulated significantly less bedding material than did the saline injected Ss. On other hand, Elavil injected Ss spent significantly more time burying and accumulated significantly more bedding material than did the saline injected Ss. No significant differences, either in terms of time spent in burying or height of accumulated bedding material, were observed during retention testing. 10 references. (Author abstract modified)

002975 de Catanzaro, Denys; Gray, D. Shaun; Gorzalka, Boris B. Gorzalka: Dept. of Psychology, University of British Columbia, 2075 Westbrook Mall, Vancouver, BC, V6T 1W5, Canada **Effects of acute central and peripheral ACTH1-24 administration on lordosis behavior.** Physiology & Behavior. 26(2):207-213, 1981.

The role of adrenocorticotropic hormone (ACTH) in the control of the lordosis reflex was studied in female Sprague-Dawley rats. Intraventricular infusion of ACTH1-24 lowered the performance of ovariectomized (ovx) and of adrenalectomized/ovariectomized (adx-ovx) estrogen primed rats. In contrast, subcutaneous injection of ACTH1-24 elevated the performance of ovx, but not of adx-ovx estrogen primed females. Spontaneous stretching, yawning, and grooming were observed after the intraventricular injection of ACTH1-24, but not after peripheral administration. Results suggest that the central effect of acute ACTH elevation differs from the peripheral effect and that the peripheral effect is mediated by the adrenals. 34 references. (Author abstract modified)

002976 Deakin, J. F. W.; Dashwood, M. R. Div. of Neurophysiology and Neuropharmacology, National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, England **The differential neurochemical bases of the behaviours elicited by serotonergic agents and by the combination of a monoamine oxidase inhibitor and L-DOPA.** Neuropharmacology. 20(2):123-130, 1981.

The role of serotonergic and dopaminergic mechanisms in the behaviors induced in rats by p-chloroamphetamine, 5-methoxy-N,N-dimethyltryptamine, and L-DOPA combined with a monoamine oxidase inhibitor was studied. Results suggest that forepaw treading, head weaving, and hind limb abduction are mediated by serotonin with no catecholamine link. Hyperreactivity and hyperactivity appear to be mediated by catecholamines. 27 references. (Author abstract modified)

002977 Deutsch, J. A. Dept. of Psychology, University of California at San Diego, La Jolla, CA 92093 **Calcitonin: aversive effects in rats?** Science. 211(4483):733-734, 1981.

The procedures used by W. Freed et al. in a study of the aversive effects of calcitonin in rats are questioned. Their study concludes that on the basis of a conditioned aversive test the reduced food intake after injections of calcitonin appears not to be the result of illness or aversive effects. A different procedure is described which utilizes a two bottle test with two novel flavors. The results of this test brings into question the results of Freed et al. 7 references.

002978 Diakow, Carol; Nemiroff, Audrey. Biology Dept., Adelphi University, Garden City, NY 11530 **Vasotocin, prostaglandin, and female reproductive behavior in the frog, Rana pipiens.** Hormones and Behavior. 15(1):86-93, 1981.

The effects of vasotocin and prostaglandin on female reproductive behavior in the frog, Rana pipiens, were studied. Receptive behavior as indicated by inhibition of the release call, was potentiated by administration of 5mcg/gbw (ip) prostaglandin E2. Arginine-8 vasotocin (1mcg/g body wt) also inhibited the release call, but its effect was delayed by a single injection of 10mcg/g body wt of the prostaglandin synthetase inhibitor, indomethacin. These results suggest that both vasotocin and prostaglandin may be involved in the manifestation of female mating behavior in R. pipiens, and that vasotocin may act, at least in part, through a mechanism that involves prostaglandin synthesis. (Author abstract modified)

002979 Dickinson, William Arthur. Southern Illinois University at Carbondale **Dose-response study of the precipitated abstinence syndrome for morphine: systemic vs periaqueductal gray naloxone. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3226-B, 1981. Ann Arbor, Univ. Microfilms No. 8102363, 122p., 1980.

The effects of systemic and periaqueductal midbrain gray (PAG) injections of naloxone on the behavior of morphine dependent rats was investigated. Eighty rats received systemic doses of 0.0, 0.05, 0.5, 5.0, or 50.0mg/kg naloxone; central PAG doses, administered to 80 rats, were 0.0, 0.1, 1.0, 10.0, and 100.0mcg/microliter isotonic saline. Postinjection testings included flinch jump and behavioral observation of withdrawal signs. A significant degree of variability in the changes on flinch jump measures was found, and although the trend was towards hyperalgesia during withdrawal this did not reach significance. Some of the behavioral components of naloxone precipitated withdrawal were more frequent and more severe following systemic naloxone while others were more severe following PAG naloxone. Still others appeared not to differ in severity and similar dose/response curves were exhibited. Results indicate that the phenomena of morphine withdrawal is most likely a reflection of both centrally (PAG) and peripherally mediated behavior changes. (Journal abstract modified)

002980 Dobry, Peggy J. K.; Piercey, M. F.; Schroeder, L. A. Upjohn Company, Central Nervous System Research, Kalamazoo, MI 49001 **Pharmacological characterization of scratching behaviour induced by intracranial injection of substance P and somatostatin.** Neuropharmacology. 20(3):267-272, 1981.

Intracranial injections of substance-P (SP) induced a reciprocal hindlimb scratching syndrome in male CF-1 mice. Scratching was also induced by the C-terminal SP hexapeptide, SP-6-11, but not by the pentapeptide, SP-7-11. Intracranial injections of biogenic amines and peptides failed to mimic the effects of SP precisely, but kainic acid and somatostatin produced weaker scratching syndromes. The effect of SP was nonspecifically antagonized by a variety of pharmacological agents. SP did not elicit scratching when given i.p. or i.v., but i.v. somatostatin did elicit scratching (with a potency similar to that of intracranial somatostatin) . Results include: 1) antagonism of reciprocal hindlimb scratching is not specific for opiates, and 2) the effect of morphine on scratching is not specifically directed against SP. 37 references. (Author abstract modified)

002981 Dourish, C. T.; Cooper, S. J. Cooper: Dept. of Psychology, University of Birmingham, Birmingham B15 2TT, England **Single or repeated administration of small doses of apomorphine on water intake and activity in water-deprived rats.** Neuropharmacology. 20(3):257-260, 1981.

Chronic treatment with small doses of apomorphine HC1 (15, 60, or 125mcg/kg/day for 10 days) stimulated water consumption in thirsty male Sprague-Dawley rats. Acute administration of apomorphine at the same dose levels did not affect drinking. Locomotor activity was stimulated by both acute and chronic apomorphine treatment. 28 references. (Author abstract modified)

002982 Dourish, Colin T.; Cooper, Steven J. Cooper: Dept. of Psychology, University of Birmingham, P.O. Box 363, Birmingham B1S 2TT, England **Effects of acute or chronic administration of low doses of a dopamine agonist on drinking and locomotor activity in the rat.** Psychopharmacology. 72(2):197-202, 1981.

The effects of acute or chronic administration of low doses of a dopamine agonist (piribedil) on drinking and locomotor activity were investigated in rats. Low doses of piribedil (0.25mg/kg to 5.0mg/kg) administered acutely produced reliable decrements in locomotor activity in thirsty and nonthirsty animals; the greatest effect occurred at the highest dose. A sequence of 10 daily injections of piribedil produced indications of the development of tolerance at the two highest doses in thirsty animals. The smallest doses used, given either acutely or chronically, produced a weak enhancement of drinking behavior within the first 15 minutes of a drinking test, as shown by a reduction in latency to drink and an increase in the amount of water consumption. Tolerance did develop with respect to drinking behavior; animals treated chronically with piribedil displayed higher levels of drinking at several dose levels when compared with acutely treated Ss. The tolerance displayed at the two highest doses could have a close affinity with that shown with regard to locomotor activity. 23 references. (Author abstract modified)

002983 Drew, William G.; DeRossett, Sarah E.; Gotsick, James E. University of Kentucky College of Medicine, Lexington, KY 40536 **An improved model of intraspecific aggression: dose-response analysis of apomorphine-induced fighting and stereotypy in the rat.** Bulletin of the Psychonomic Society. 17(1):53-56, 1981.

A paradigm more sensitive and specific than the original apomorphine model proposed by Senault was employed to measure intraspecific aggression in the rat. Several behavioral measures provided detailed descriptions of aggressive and nonaggressive behaviors. Several new aggressive responses not previously attributed to apomorphine are noted. Graded doses of apomorphine were administered to determine the qualitative and quantitative dose response relationships produced by apomorphine on both aggressive and nonaggressive behaviors. It is reported that maximum fighting times were obtained at apomorphine doses of 2.5 and 5.0mg/kg. 11 references. (Author abstract)

002984 Driscoll, Peter; Baettig, Karl. Institut fuer Verhaltenswissenschaft, ETHZ, CH-8092 Zurich, Switzerland **Selective inhibition by nicotine of shock-induced fighting in the rat.** Pharmacology Biochemistry and Behavior. 14(2):175-179, 1981.

The frequency of shock induced fighting, posturing, and no reaction (running/jumping or freezing) after acute SC injections of 0, 0.1, 0.2, and 0.4mg/kg nicotine, was measured in 38 pairs of male and 12 pairs of female rats. Sensitivity to footshock was also measured, at the same nicotine doses, in males. Nicotine inhibited shock induced fighting in 32 pairs of high frequency fighting males in a dose dependent fashion, with fighting being gradually replaced by posturing at the 0.1 and 0.2mg/kg doses. There was a significant increase in the no reaction category only at 0.4mg/kg, indicating that reduced activity may have been partly responsible for the reduction in fighting seen at that dose. None of the doses had a significant effect on sensitivity to footshock. Nicotine had no effect on shock induced fighting in the six low frequency fighting male pairs, and affected the female pairs only at the 0.4mg/kg level, where fighting was also decreased due to an increase in the no reaction category. It is concluded that small doses of nicotine, under favorable conditions, are capable of inhibiting shock induced fighting in rats without altering shock sensitivity or depressing activity. 46 references. (Author abstract)

002985 Dunn, Adrian J.; Childers, Steven R.; Kramarcy, Neal R.; Villiger, John W. Dept. of Neuroscience, University of Florida College of Medicine, Gainesville, FL 32610 **ACTH-induced grooming involves high-affinity opiate receptors.** Behavioral and Neural Biology. 31(1):105-109, 1981.

Naloxazone, an irreversible inhibitor of high affinity opiate receptors was used to test whether excessive grooming in mice following intracerebroventricular ACTH involves interaction with high affinity of opiate receptors. ACTH induced grooming was blocked 16 hours following naloxazone but not naloxone. At this time morphine induced antinociception measured in the tail immersion test was present in naloxone but not naloxazone treated mice. The deficit caused by naloxazone was not permanent and 4 days later, ACTH again elicited excessive grooming. These results together with other published data suggest that ACTH induces excessive grooming by interaction with high affinity cerebral opiate receptors. 10 references. (Author abstract)

002986 Dunstan, Robin; Broekkamp, Chris L.; Lloyd, Kenneth G. Lloyd: Synthelabo-L.E.R.S., Dept. of Neuropharmacology, 31, Avenue Paul Vaillant Couturier, F-92220 Bagneux, France **Involvement of caudate nucleus, amygdala or reticular formation in neuroleptic and narcotic catalepsy.** Pharmacology Biochemistry and Behavior. 14(2):169-174, 1981.

The involvement of caudate nucleus, amygdala, or reticular formation in neuroleptic and narcotic catalepsy was studied. Local injection of haloperidol into the caudate nucleus produced catalepsy in contrast to the weak effects of morphine injected at the same site. Injection of either haloperidol or morphine into the amygdala did not have any cataleptogenic effect. Both haloperidol and morphine produced catalepsy when injected into the reticular formation. Naloxone injected into the reticular formation completely reversed the catalepsy following intraperitoneal morphine but not haloperidol. Pretreatment with alpha-methyl-p-tyrosine potentiated the effect of haloperidol injected into either the reticular formation or caudate nucleus. Phentolamine, but not lignocaine or metergoline, injected into the reticular formation also caused a cataleptic response. The results confirm the caudate nucleus as a site for haloperidol catalepsy and in addition, suggest the reticular formation as a primary site for morphine catalepsy and a secondary site for haloperidol catalepsy; additionally, a noradrenergic modulation of catalepsy may occur within this brainstem region. 30 references. (Author abstract modified)

002987 Eichelman, Burr S., Jr. Dept. of Psychiatry, University of Wisconsin, Madison, WI 53706 **Drug regimens facilitating aggression: behavior, amine, and receptor alterations.** Psychopharmacology Bulletin. 17(1):58-60, 1981.

Studies of drug regimens which facilitate aggression are described, and the behavioral, amine, and receptor alterations caused by these drugs are discussed. Studies confirm previous findings that catecholamines play a facilitatory role in the modification of aggressive behavior and serotonin systems play an inhibitory role; however, substantial differences among animal models and between the effects of acute and chronic drug regimens are demonstrated. It is cautioned that the role of serotonin in predatory aggression must be carefully dissected from caloric or protein deficiencies which also alter predatory aggression in both the rat and mouse. 11 references. (Author abstract modified)

002988 Ellison, Gaylord; Nielsen, Erik B.; Lyon, Melvin. Dept. of Psychology, University of California, 405 Hilgard Ave., Los Angeles, CA 90024 **Animal model of psychosis: hallucinatory behaviors in monkeys during the late stage of continuous amphetamine intoxication.** Journal of Psychiatric Research. 16(1):13-22, 1981.

Hallucinatory behaviors in monkeys were examined after silicone capsules containing d-amphetamine base were implanted subcutaneously in seven monkeys. All monkeys were sleepless for a number of days, initially engaging in highly idiosyncratic episodes of motor stereotypies or prolonged bouts of staring. This was followed by a period of less focused activity where fragments of the initial stereotypies appeared. On the fourth to sixth day after capsule implanation several new behaviors developed. There were increases in sudden orienting responses and motor dyskinesias such as limb tremors and oral protrusions. At about the same time discrete episodes of hallucinatory behaviors appeared, including at different times attacks, sudden fleeing responses, capturing movements by the hands in midair, and excited grooming episodes of parasitosis. This late stage of continuous amphetamine administration in monkeys is similar to the final stages of amphetamine psychosis, which in humans is a close drug model of paranoid schizophrenia. 21 references. (Author abstract modified)

002989 Faustman, William; Fowler, Stephen; Walker, Cynthia. Fowler: Dept. of Psychology, University of Mississippi, University, MS 38677 **Time course of chronic haloperidol and clozapine upon operant rate and duration.** European Journal of Pharmacology. 70(1):65-70, 1981.

The effects of haloperidol and clozapine on operant response rate and average response duration were determined in male Sprague-Dawley rats responding under a fixed-ratio 10 schedule of food reinforcement. Haloperidol (0.5mg/kg i.p.) was given 2.5, 5.0, 7.5, and 10 hours prior to testing, and clozapine (5.9mg/kg i.p.) was given 1.0, 2.0, 3.0, and 4.0 hours before testing. For both drugs, the time since injection produced significant effects on rate and duration: rate increased and duration decreased as a function of time after injection. Haloperidol tended to have a greater effect than clozapine on response duration. 13 references. (Author abstract modified)

002990 Fernando, J. C. R.; Curzon, G. Dept. of Neurochemistry, Institute of Neurology, 33, John's Mews, London WC1N 2NS, England **Behavioural responses to drugs releasing 5-hydroxytryptamine and catecholamines: effects of treatments altering precursor concentrations in brain.** Neuropharmacology. 20(2):115-122, 1981.

The effects of amino acids that alter brain tryptophan or tyrosine concentrations on behavioral responses to p-chloroamphetamine, fenfluramine, and d-amphetamine were studied in male Sprague-Dawley rats. Tryptophan increased the tremor induced by p-chloroamphetamine and the backward walking induced by fenfluramine, but did not alter the drugs' other behavioral effects. Tryptophan altered some but not all of the behaviors evoked by d-amphetamine. Behavioral responses dependent on serotonin or catechloamine release were not altered by tyrosine or valine. Results are discussed in relation to the regulation of serotonin and dopamine synthesis and the behavioral interactions of these transmitters. 29 references. (Author abstract modified)

002991 File, Sandra E.; Clarke, Anthony. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Exploration and motor activity after intraventricular ACTH, morphine and naloxone.** Behavioural Brain Research. 2(2):223-227, 1981.

The effects of intraventricular adrenocorticotrophin (ACTH), morphine, and naloxone on exploration and motor activity were investigated. Intraventricular injection of morphine (5mcg) and ACTH (2.5mcg) reduced the time spent head dipping and the number of head dips made by rats during a 10 minute trial in a holeboard. These effects were reversed by naloxone (2.0mg/kg), in spite of the fact that naloxone alone also reduces these measures of exploration. None of the drugs or drug combinations tested significantly reduced locomotor activity. Results are discussed in relation to the action of ACTH on opiate receptors. 20 references. (Author abstract modified)

002992 Freed, William J.; Bing, Lloyd A.; Wyatt, Richard Jed. Adult Psychiatry Branch, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Calcitonin: aversive effects in rats?** Science. 211(4483):734, 1981.

A response is offered to the criticisms of J. A. Deutsch concerning the ability of calcitonin to produce conditioned taste aversion in rats. It is reported that several studies were performed using those procedures suggested by Deutsch. However, these experiments still failed to produce a statistically significant conditioned taste aversion with calcitonin. It is still maintained that any sickness produced by calcitonin is insufficient to account for the inhibition of feeding. 5 references.

002993 Freed, William J.; Wyatt, Richard Jed. Adult Psychiatry Branch, Division of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Impairment of instrumental learning in rats by glutamic acid diethyl ester.** Pharmacology Biochemistry and Behavior. 14(2):223-226, 1981.

The effects of glutamic acid diethyl ester (GDEE), a partially effective antagonist of glutamate induced neuronal excitations, on instrumental learning in rats were investigated. GDEE was administered prior to an instrumental conditioning task involving food reinforcement. A profound impairment of learning was produced in animals receiving 240 or 480mg/kg of GDEE. Performance was not impaired by GDEE in rats that had previously learned the task. These findings support suggestions that central excitatory processes play an important role in learning phenomena, in particular when these learning phenomena involve acquisition of new behavioral patterns. 40 references. (Author abstract modified)

002994 Friedman, Howard J.; Jen, Ming-Feng; Kang, Jaw Chang; Lee, Nancy M.; Loh, Horace H. Lee: Langley Porter Psychiatric Institute, University of California, San Francisco, CA 94143 **Dynorphin: a possible modulatory peptide on morphine or beta-endorphin analgesia in mouse.** European Journal of Pharmacology. 69(3):357-360, 1981.

The interaction of dynorphin-(1-13) with analgesic opioids was demonstrated in male ICR mice in the tail flick test. Intracerebroventricular (i.c.v.) injection of 20 or 40mcg dynorphin-(1-13) had no analgesic effect itself, but attenuated the analgesia produced by morphine (2.0, 8.0, or 12.0mcg i.c.v.). Dynorphin-(1-13) potentiated analgesia induced by a 1.0mcg i.c.v. dose of beta-endorphin, but attenuated the analgesic effect of 4.0 or 6.0 i.c.v. beta-endorphin. A shorter portion of the dynorphin peptide, dynorphin-(1-9), had no analgesic effect itself and did not alter analgesia induced by beta-endorphin. Dynorphin-(1-13) had no effect on analgesia induced by the Sandoz compound FK33824, a met-enkephalin analogue. 6 references. (Author abstract modified)

002995 Fuller, R. W.; Snoddy, H. D.; Mason, N. R.; Owen, J. E. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, IN 46285 **Disposition and pharmacological effects of m-chlorophenylpiperazine in rats.** Neuropharmacology. 20(2):155-162, 1981.

The effects of 1-(m-chlorophenyl)piperazine (CPP), a metabolite of the antidepressant trazodone, on central serotonergic systems in male Wistar rats were determined. Results suggested that CPP acts as a direct serotonin agonist. It is suggested that the serotonin receptor agonist activity of CPP may account for the clinical antidepressant effects of trazodone. 34 references. (Author abstract modified)

002996 Fung, Yiu Kai. Ohio State University **The role of calcium and dopamine membrane carrier in mediating the behavioral and biochemical effects of amphetamine. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2575-B, 1981. Ann Arbor, Univ. Microfilms No. 8100153, 121p., 1980.

The role of calcium in mediating the behavioral effects of amphetamine was evaluated by the removal of calcium from extracellular space and possibly the tissue of mice striatum using ethylene glycol-bis-beta-aminoethylether,N-N'-tetraacetic acid (EGTA). The intrastriatal administration of EGTA or any other agents used did not by itself elicit circling behavior in mice lesioned with 6-hydroxydopamine in the right striatum. The effect of a variety of compounds on the circling behavior induced by the subsequent systemic injection of amphetamine was examined. EGTA inhibited the amphetamine induced circling. This effect of EGTA could be prevented by adding calcium to the EGTA solution, confirming that the effect of EGTA is due to the removal of calcium. While dopamine (DA) uptake blocking agents inhibit all the biochemical effects of amphetamine, EGTA only inhibits the stimulation of DA synthesis. Thus, EGTA may inhibit the behavioral effect of amphetamine by a different mechanism than the DA uptake inhibitors. Findings confirm the importance of calcium and the dopamine membrane carrier in mediating the behavioral and biochemical effects of amphetamine and that the mechanism of action of amphetamine is dependent on the release of a pool of DA that is supplied by new synthesis. This process of DA synthesis is dependent on extracellular calcium. (Journal abstract modified)

002997 Furman, J. M.; O'Leary, D. P.; Wolfe, J. W. O'Leary: Eye and Ear Hospital, 230 Lothrop St., Room 925, Pittsburgh, PA 15213 **Changes in the horizontal vestibulo-ocular reflex of the rhesus monkey with behavioral and pharmacological alerting.** Brain Research. 206(2):490-494, 1981.

Alterations in the dynamic characteristics of the horizontal vestibulo/ocular reflex of adolescent rhesus monkeys by changes in the animals' states of arousal were studied using linear system analysis employing both single frequency sinusoidal and white noise rotational stimulations. Arousal changes were induced by a behavioral task and/or the administration of amphetamines. Results indicate that highly alert animals display vestibulo/ocular reflex gains significantly different from less alert animals. Specifically, the gain of the vestibulo/ocular reflex is closer to unity over a wider range of frequencies in more alert animals. These changes were independent of the method used to maintain a high level of arousal. 10 references. (Author abstract modified)

002998 Gallagher, Michela; Kapp, Bruce S. Dept. of Psychology, Davie Hall 013A, University of North Carolina, Chapel Hill, NC 27514 **Effect of phentolamine administration into the amygdala complex of rats on time-dependent memory processes.** Behavioral and Neural Biology. 31(1):90-95, 1981.

The effects of alpha-adrenergic antagonist phentolamine on memory processes following intracranial administration into the amygdala complex were examined in Sprague-Dawley rats. The administration of phentolamine was observed to alter memory processes in a time dependent manner. Bilateral administration of phentolamine (8.5nmole) into the amygdala immediately after training significantly increased retention of passive avoidance conditioning. Delayed administration of the same dose 6 hours after training did not significantly alter retention. In addition, whereas posttraining administration of the beta-adrenergic antagonist propranolol (34.Onmole) into the amygdala significantly decreased retention, concurrent administration of phentolamine (8.5nmole) and propranolol (34.Onmole) resulted in normal retention. The effects of alpha-adrenergic and beta-adrenergic antagonist administration on memory processes are discussed in terms of a possible opposing effect of these agents on norepinephrine function within the amygdala complex. 10 references. (Author abstract)

002999 Gerber, Gary J.; Bozarth, Michael A.; Wise, Roy A. Center for Research on Drug Dependence, Dept. of Psychology, Concordia University, Montreal, Quebec, Canada H3G 1M8 **Small-dose intravenous heroin facilitates hypothalamic self-stimulation without response suppression in rats.** Life Sciences. 28(5):557-562, 1981.

Intravenous heroin at 10mcg/kg and 30mcg/kg produced an immediate increase in rates of lever-pressing for electrical stimulation of the lateral hypothalamus, while 100mcg/kg produced brief suppression in some rats followed by reliable response rate increases in all rats. The duration of response facilitation increased with dose and corresponded to the duration of the interinfusion interval found in self-administration experiments. These data indicate correspondence between the reinforcing and the self-stimulation facilitation effects of heroin in relation to dose and time course parameters, and fit with the view that narcotic facilitation of self-stimulation reflects the reinforcing value of the drugs. 10 references. (Author abstract)

003000 Gerber, Gary J.; Sing, John; Wise, Roy A. Wise: Center for Research on Drug Dependence, Dept. of Psychology, Concordia University, Montreal, Quebec, Canada H3G 1M8 **Pimozide attenuates lever pressing for water reinforcement in rats.** Pharmacology Biochemistry and Behavior. 14(2):201-205, 1981.

The effects of pimozide on water reinforced lever-pressing by thirsty rats were examined to test the generality of neuroleptic effects on consumatory behavior. A low dose of pimozide (0.5mg/kg) did not significantly attenuate responding until the fifth session. A higher dose (1.0mg/kg) attenuated responding on all test occasions, with residual responding decreasing progressively across repeated drug sessions. Responding in the pimozide conditions was never less than that of the nonreinforced control group. Responding in each condition was strongest in the early minutes of a session. After five sessions, rats were switched from the pimozide condition to the nonreinforced condition (or vice versa) for one additional test day. Decreased responding continued for rats transferred from nonreinforcement to pimozide though not for rats transferred from pimozide to nonreinforcement. These data suggest a general role for brain dopamine in behavior; they reflect the same patterns as have been seen with food reinforcement and with several centrally acting reinforcers. 18 references. (Author abstract modified)

003001 Gisquet-Verrier, Pascale. Centre National de la Recherche Scientifique, Lab. de Physiologie Nerveuse, Dept. de Psychophysiologie, F-91190 Gif-sur-Yvette, France **Accelerated extinction after post-trial halothane anaesthesia in rats: an aversive effect.** Physiology & Behavior. 26(2):223-231, 1981.

In male Sprague-Dawley rats trained in straight alley, modified K-maze, and barpress learning tasks, extinction was accelerated by immediate posttrial treatment with halothane. This effect was not due to motor impairment and was not observed when halothane was given 2 hours after the trial. No amnesic component was associated with a single halothane treatment, but aversive effects were observed after repeated halothane administration. Results suggest that the effects of halothane on retention may be due to aversive rather than amnesic properties. 34 references. (Author abstract modified)

003002 Glick, Stanley D.; Weaver, Linda M.; Meibach, Richard C. Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, One Gustave L. Levy Place, New York, NY 10029 **Amphetamine-induced rotation in normal cats.** Brain Research. 208(1):227-229, 1981.

Amphetamine elicited dose related rotation (circling behavior) in nine naive cats is reported. All cats also rotated, at lower rates, during nondrug sessions. The direction of rotation was consistent for each cat, with six cats rotating to the right and three to the left. Results extend the generality of previous findings involving rodents and suggest that an endogenous asymmetry in striatal dopamine activity may be a common characteristic of many animal species. An asymmetry in striatal dopaminergic function has not yet been directly demonstrated in man; however, a recent report of lateralized neuroleptic induced dyskinesias suggests that such an asymmetry will soon be found. 16 references. (Author abstract modified)

003003 Goett, James Michael; Kay, Edwin J. Kay: Dept. of Psychology, Lehigh University Chandler-Ullmann No. 17, Bethlehem, PA 18015 **Lithium chloride and delta-9-THC lead to conditioned aversions in the pigeon.** Psychopharmacology. 72(2):215-216, 1981.

Conditioned aversive effects of delta9-tetrahydrocannabinol (THC) and lithium chloride (LiC1) were demonstrated in pigeons. Pigeons injected with 0.15M LiC1 showed a reduction in preference for red water compared to pigeons injected with NaC1. Pigeons injected with 2.0mg/kg of THC showed a decreased preference for red water. It was necessary to habituate the pigeons to the novel color of the water, which is in contrast to the usual report that a novel stimulus is more effective in the aversive conditioning literature. 6 references. (Author abstract modified)

003004 Gomita, Yutaka; Ueki, Showa. Dept. of Pharmacology, Daiichi College of Pharmaceutical Sciences, Fukuoka 815, Japan **behavior and the effect of benzodiazepines.** Pharmacology Biochemistry and Behavior. 14(2):219-222, 1981.

The effects of benzodiazepines on behavior of rats in a conflict situation established by combining foot shock punishment with brain stimulation were investigated. Diazepam caused a marked increase in the lever-pressing response in the punished period without affecting the unpunished response. Bromazepam also caused an increase in the lever-pressing response in the punished period and a decrease of the punished response. These results indicate that a conflict situation based on self-stimulation behavior is useful for the evaluation of antianxiety action. 11 references. (Author abstract modified)

003005 Gonzalez, Larry P.; Ellinwood, Everett H., Jr. Dept. of Physiology and Biophysics, University of Illinois Medical Center, P.O. Box 6998, Chicago, IL 60680 **Amphetamine-induced motility and nigrostriatal impulse flow.** Brain Research. 208(1):223-226, 1981.

The effects of altered nigrostriatal impulse flow on amphetamine induced behaviors were investigated in rats. Systemic amphetamine produced a general increase in power at all observed frequencies, with a dose dependent increase in motility in the 8 to 10 Hz frequency band. These responses, a general increase in power and the occurrence of an 8 to 10 Hz peak, were not significantly altered by the intranigral administration of saline or apomorphine, nor did such treatment alone affect motility. Results question the involvement of nigrostriatal impulse flow in the effects of amphetamine on motility, and they suggest the need for further investigation into the function of the nigrostriatal dopaminergic neurons and their relationship to the mechanism of action of amphetamine. 19 references. (Author abstract modified)

003006 Haber, Suzanne; Barchas, Patricia R.; Barchas, Jack D. Dept. of Psychology, Massachusetts Institute of Technology, 79 Amherst St., Cambridge, MA 02139 **A primate analogue of amphetamine-induced behaviors in humans.** Biological Psychiatry. 16(2):181-196, 1981.

The effects of amphetamine on individual and social behaviors were studied in two colonies of rhesus monkeys. After an initial baseline period, each animal, in turn, received low chronic drug administration for 3 weeks. Between each drug period new baseline data were collected. During amphetamine administration, there was a significant increase in the following behaviors: time spent in tense" postures, frequency of orienting, and frequency of agonistic behaviors. In addition, significant changes were seen in the time spent in proximity with other members of the group. The results are discussed both in terms of across animal changes and with regard to social factors, rank in the hierarchy, and affiliative relationships. 16 references. (Author abstract)

003007 Haber, Suzanne; Kraemer, Helena. Dept. of Psychology and Brain Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **A research paradigm to investigate the effect of manipulation on social behavior in groups.** Journal of Psychiatric Research. 16(1):23-28, 1981.

A paradigm for the design and analysis of studies of the effects of biological manipulation on the behavior of animals living in social groups is presented. Such studies are typically based on small sample sizes but such small sample designs are subject to both bias and to low power. The proposed design isolates bias due to time trends, and because of its systematic construction, minimizes bias due to other factors. Use of nonparametric analytic procedures reduces the possibility of statistical biases. Because of the requirement of acceptable reliability of observation at the outset and of repeated measures in the design, the power of the procedure is substantially amplified. This procedure is illustrated in a study of the behavioral effects of chronic amphetamine treatment in monkeys on the frequency of sitting tense, a paranoid like behavior. 8 references. (Author abstract modified)

003008 Hara, Shuichi; Satoh, Tetsuo; Kitagawa, Haruo. Satoh: Laboratory of Biochemical Pharmacology and Biotoxicology, Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan **Induction of hypersensitivity of brain by hydralazine treatment in rats.** Research Communications in Chemical Pathology and Pharmacology. 31(2):251-257, 1981.

Hypnosis induced by i.p. injection of 80mg/kg hexobarbital or intracerebroventricular injection of 1mg phenobarbital in male Wistar rats was prolonged by pretreatment with hydralazine (10mg/kg i.p.). Brain concentration of hexobarbital was lower in animals treated with hydralazine than in controls, but liver microsomal drug metabolizing enzyme activities were not altered by hydralazine. Results suggest that hydralazine increases the sensitivity of the brain to barbiturates. 6 references. (Author abstract modified)

003009 Henning, James M.; Zentall, Thomas R. Zentall: Dept. of Psychology, University of Kentucky, Lexington, KY 40506 **Imitation, social facilitation, and the effects of ACTH4-10 on rats' bar-pressing behavior.** American Journal of Psychology. 94(1):125-134, 1981.

The effects of ACTH4-10 on rats' imitation learning was examined during the acquisition and extinction of a bar-press response for water reinforcement. Ss were exposed to a bar-pressing conspecific, an experimentally naive conspecific, or an empty box during bar-press acquisition. Each S was then exposed to one of the same three conditions during extinction. A 80mcg dose of ACTH4-10 was given to half of the Ss in each group prior to observation. Performance differences during acquisition were generally small, but significant performance differences during extinction were found. Social facilitation was indicated, and an imitation effect was also found. However, there were no significant effects of the hormone, relative to saline controls. 20 references. (Author abstract modified)

003010 Herling, Seymore. University of Michigan **An analysis of specificity of drug-induced changes in drug-reinforced responding. (Ph.D. dissertation).** Dissertation Abstracts International. 41(9):3620-B, 1981. Ann Arbor, Univ. Microfilms No. 8106153, 141p., 1980.

Lever-pressing was maintained in rhesus monkeys by the presentation of food and, in alternate periods of each daily session, by the intravenous delivery of either cocaine or codeine. At appropriate doses, cocaine and codeine maintained rates of responding as high as those maintained by food. Chlorpromazine decreased responding maintained by low to intermediate doses of cocaine. Injections of naltrexone produced a dose related shift to the right in the rate decreasing effect of codeine. It is suggested that the effect of naltrexone on codeine reinforced responding are relatively more specific than the effects of chlorpromazine on cocaine reinforced responding. (Journal abstract modified)

003011 Herman, Barbara H.; Panksepp, Jaak. Panksepp: Dept. of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Ascending endorphin inhibition of distress vocalization.** Science 211(4486):1060-1062, 1981.

The effects of naloxone and periventricular gray (PVG) stimulation on distress vocalizations elicited from the septum/preoptic area and the dorsomedial thalamus were analyzed in adult albino guinea-pigs. Both forebrain derived vocalizations were increased by systemic administration of naloxone and were inhibited by analgesic periventricular gray stimulation. Naloxone blocked the inhibitory effects of the analgesic stimulation on thalamic vocalizations. Stimulation of nonanalgesic mesencephalic sites in close proximity to the periventricular gray increased the anterior elicited vocalizations. These data provide evidence for ascending endorphin mediated inhibition of excitatory forebrain sites for distress vocalization. 11 references. (Author abstract modified)

003012 Herndon, James G.; Allen, William C.; Blakely, Randy D. Division of Neurobiology, Yerkes Regional Primate Research Center, Emory University, Atlanta, GA 30322 **Increases in testosterone levels and in copulatory behavior of male rhesus monkeys following treatment with human chorionic gonadotrophin.** Hormones and Behavior. 14(4):337-347, 1980.

The sexual behavior of five male rhesus monkeys were observed before, during, and after administration of human chorionic gonadotropin (HCG) sufficient to induce increases in serum testosterone. Each S received 12 20 min pair tests with an estrogen implanted ovariectomized female during pretreatment, treatment, and posttreatment phases. Grooming, mount latency, and ejaculation frequency, as well as other behavioral measures, were unaffected by hormone treatment. Latency to ejaculation decreased by 40% and mount rate increased by 71% during hormone administration. Sexual presentations by the female decreased by 39% and limb shaking decreased by 55% during treatment. These findings demonstrate that increases in testosterone secretion subsequent to gonadotrophin injection in intact male rhesus monkeys can produce significant alterations in male and female sexual behavior. 17 references. (Author abstract modified)

003013 Hill, Ronald C.; Maurer, Richard; Buescher, Heinz-Hermann; Roemer, Dietmar. Preclinical Research Dept., Sandoz Ltd., CH-4002 Basel, Switzerland **Analgesic properties of the GABA-mimetic THIP.** European Journal of Pharmacology. 69(2):221-224, 1981.

The analgesic properties of the muscimol analogue 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) were compared with those of baclofen, morphine, and muscimol in rats, mice, and rhesus monkeys. THIP was active orally and parenterally and showed a qualitative resemblance to muscimol in action. Quantitatively, THIP and baclofen were 2 to 3 times less potent than morphine and 5 to 15 times less potent than muscimol. The analgesic effects of THIP, baclofen, and muscimol were not reversed by naloxone or bicuculline. 11 references. (Author abstract modified)

003014 Hoddes, E. S. St. Mary's Hospital, Medical Center, San Francisco, CA **Effect of growth hormone on memory in mice.** Sleep. 1:287-297, 1979.

The effects of growth hormone (GH) on long-term memory were investigated in two experiments using a common paradigm. Mice received massed training on a discrimination task and were injected with GH or control substances before and/or after training. Retention was measured 4 weeks later. In Experiment 1, different groups were injected with either GH or saline at five time points relative to original learning (OL). The results showed a significant quadratic trend in the form of a U-shaped curve for the GH injected groups at retention. Maximal retention was observed in the 90 minute pre-OL and 30 minute post-OL injection groups. Poorest retention was shown by the 5 minute pre-OL injection group. In Experiment 2, GH, saline, and thyroid stimulating hormone were administered at 90 minutes and 5 minutes pre-OL. The results again showed a severe drop in retention when GH was administered 5 minutes before OL. The overall findings indicate a selectively GH induced suppression of memory when GH is administered in close proximity to OL. As the time lapse between injection of drug and the learning task increases, the inhibitory effect on memory is reversed. (Journal abstract modified)

003015 Hoebel, Bartley G.; Hernandez, Luis; Monaco, Anthony P.; Miller, William C. Dept. of Psychology, Princeton University, Princeton, NJ 08544 **Amphetamine-induced overeating and overweight in rats.** Life Sciences. 28(1):77-82, 1981.

The effects of a single large dose of d-amphetamine on food intake and bodyweight maintenance were investigated. Female rats given a large dose of d-amphetamine displayed transient anorexia and loss of weight as one would expect. A week later, after their food intake and weight had returned to baseline, they began to overeat and gain weight. Within three weeks they were eating 7% more than normal. They became 3% overweight with a 5% increase in body fat. They hyperphagia persisted for two months. Thus, amphetamine, an appetite suppressant and sympathomimetic drug, can cause prolonged hyperphagia and mild obesity with delayed onset following a single overdose. 13 references. (Author abstract modified)

003016 Hunt, Glenn E.; Atrens, Dale M.; Johnson, Gordon F. S. Dept. of Psychiatry, University of Sydney, Sydney, 2006, N.S.W., Australia **The tetracyclic antidepressant mianserin: evaluation of its blockade of presynaptic alpha-adrenoceptors in a self-stimulation model using clonidine.** European Journal of Pharmacology. 70(1):59-63, 1981.

The effects of mianserin, a tetracyclic antidepressant, were investigated in male Sprague-Dawley rats in a shuttlebox self-stimulation model sensitive to alpha-adrenergic drugs. Mianserin (2.5 to 40.Omg/kg i.p.) not only failed to enhance hypothalamic self-stimulation, but produced a selective inhibition of reward. Mianserin also failed to reverse the inhibitory effects of clonidine on self-stimulation. Results suggest that mianserin is not a selective antagonist of presynaptic alpha-adrenoceptors. 23 references. (Author abstract modified)

003017 Irving, S. M.; Goy, R. W.; Haning, R. V.; Davis, G. A. Davis: Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, WI 53706 **Prostaglandins, clonidine and sexual receptivity in the guinea-pig.** Brain Research. 204(1):65-77, 1981.

The effects of prostaglandins on sexual receptivity in the guinea-pig were investigated. Prostaglandins E1 and F2alpha suppressed lordosis in ovariectomized guinea-pigs brought into estrus with estradiol benzoate and progesterone. Pretreatment with clonidine prevented this action of the prostaglandins, but if the animals were first given prostaglandin and allowed to go out of estrus, then clonidine did not restore lordosis. In a previous study, it was found that the abbreviation of estrus induced by copulation was also blocked by clonidine, again only if it were given before the inhibitory treatment. These results suggest that prostaglandin, perhaps released from the female reproductive tract, could mediate the inhibitory effect of copulation, and radioimmunoassays of prostaglandin F2alpha and its principal metabolite PGFM revealed substantial elevations in the concentrations of these materials in trunk blood after copulation. The possibility that prostaglandins may suppress sexual receptivity by interfering with an alpha-adrenergic mechanism is discussed. 39 references. (Author abstract modified)

003018 Jacobs, Barry L.; Heym, James; Trulson, Michael E. Program in Neuroscience, Dept. of Psychology, Princeton University, Princeton, NJ 08544 **Cats develop tolerance to d-amphetamine's effects upon locomotion and stereotyped behaviors.** European Journal of Pharmacology. 69(3):353-356, 1981.

Administration of d-amphetamine sulfate (7.5mg/kg i.p) twice daily to cats produced an initial large increase in locomotion and behavioral stereotypy. However, both measures showed large decreases when the d-amphetamine regimen was continued for more than 3 days. It is suggested that tolerance to the behavioral effects of d-amphetamine is due to the concomitant decrease in presynaptic stores of dopamine and norepinephrine. 7 references. (Author abstract modified)

003019 Jones, D. L.; Mogenson, G. J.; Wu, M. Dept. of Physiology, Faculty of Medicine, University of Western Ontario, London, Ontario, Canada N6A 5C1 **Injections of dopaminergic, cholinergic, serotoninergic and GABAergic drugs into the nucleus accumbens: effects on locomotor activity in the rat.** Neuropharmacology. 20(1):29-37, 1981.

The effects on locomotor activity in the rat of injections of dopaminergic, cholinergic, serotoninergic, and GABAergic drugs into the nucleus accumbens were investigated. Dopamine (which elicited locomotor activity) was injected together with cholinergic, serotonergic, and GABAergic agonists and antagonists to investigate the possible contribution to locomotor activity of these putative neurotransmitters. Carbachol elicited a transient enhancement of dopamine stimulated activity. Atropine attenuated carbachol stimulated enhancement but did not attenuate dopamine stimulated activity. Serotonin attenuated dopamine stimulated activity. The administration of GABA elicited a bimodal response in locomotion. Results suggest that there is not a cholinergic interneuron on the dopamine stimulated pathway subserving locomotion but that both cholinergic and serotoninergic projections may modulate locomotor activity. Further, they suggest that such modulation must be at least one inhibitory interneuron away from the dopamine synapse on the locomotor pathway. In addition, these results suggest a direct influence of GABAergic interneurons on the pathway subserving locomotor activity within the nucleus accumbens. 56 references. (Author abstract modified)

003020 Kameyama, T.; Ukai, M. Dept. of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Multi-dimensional analyses of behavior in mice treated with alpha-endorphin.** Neuropharmacology. 20(3):247-250, 1981.

A multidimensional behavioral analyzer based on a capacitance system was used to study the effects of intracerebral injection of alpha-endorphin on spontaneous locomotor activity in male ddY mice. Alpha-endorphin (20mcg) caused a marked but transient increase in linear locomotion, which could be reversed by naloxone. Intracerebral injection of alpha-endorphin also facilitated the hyperactive movements induced by apomorphine and methamphetamine, suggesting that alpha-endorphin may enhance dopaminergic activity. 19 references. (Author abstract modified)

003021 Kantak, Kathleen M.; Hegstrand, Linda R.; Eichelman, Burr. Eichelman: Psychiatry Service, William S. Middleton Memorial Veterans Hospital, 2500 Overlook Terrace, Madison, WI 53705 **Aggression-altering effects of cyclic AMP.** Neuropharmacology. 20(1):79-82, 1981.

Dibutyryl cyclic AMP, infused intraventricularly in rats and mice, was found to produce dose dependent increases in cyclic AMP and dose dependent decreases in shock induced rat fighting and isolation induced mouse fighting and cricket attack, but not in cricket killing or mousekilling. Reduction in aggression with 25mcg was not related to sedation or motor disturbance since motor activity counts were normal, as were whole brain levels of serotonin, norepinephrine, and dopamine. These data are consistent with the hypothesis that neuronal cyclic AMP, in part, functions as a second messenger mediating the effects of released neurotransmitters in regulating behavior. 10 references. (Author abstract modified)

003022 Karson, Craig N.; Staub, Richard A.; Kleinman, Joel E.; Wyatt, Richard Jed. Adult Psychiatry Branch, Division of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Blink rates and receptor supersensitivity.** Neuropharmacology. 20(1):91-93, 1981.

The dose response of blink rates to apomorphine was studied before and after haloperidol treatment in four monkeys. Seven days following haloperidol discontinuation, there was no alteration of baseline blink rates but the blink rate response to low dose apomorphine was significantly increased indicating that haloperidol treatment had sensitized the animals. Because the major action of neuroleptics on dopamine neurons is thought to be postsynaptic blockade, it is speculated that postsynaptic supersensitivity of dopamine receptors is the etiology of increased sensitivity in these monkeys. It is claimed that blink rates, because they are easily quantifiable, seem to be a promising tool in the study of neurochemical mechanisms. 10 references. (Author abstract modified)

003023 Karson, Craig N.; Staub, Richard A.; Kleinman, Joel E.; Wyatt, Richard J. Lab. of Clin. Psychopharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Drug effect on blink rates in rhesus monkeys: preliminary studies.** Biological Psychiatry. 16(3):249-254, 1981.

Various drugs that alter central monoamine activity were given to rhesus monkeys to determine the effects on blink rates. Chronic pargyline treatment raised the mean plus or minus standard deviation blink rate slightly to 18.2 plus or minus 5.3 blinks/90 sec. When phenylethylamine was added to chronic pargyline treatment, blinks increased from a baseline of 16.8 plus or minus 7.6 blinks/90 sec to 37 plus or minus 15 blinks/90 sec. Apomorphine (.36mg/kg) raised blinks from a baseline of 12.2 plus or minus 2.8 blinks/90 sec to 41.9 plus or minus 10.3 blinks/90 sec and reversed a decrease in blinking caused by haloperidol. The neurochemical basis of blinking and implications for tardive dyskinesia are discussed. 12 references. (Author abstract)

003024 Kasamatsu, Takuji; Pettigrew, John D.; Ary, Marylouise. Division of Biology, 216-76 Beckman Laboratories, California Institute of Technology, Pasadena, CA 91125 **Cortical recovery from effects of monocular deprivation: acceleration with norepinephrine and suppression with 6-hydroxydopamine.** Journal of Neurophysiology. 45(2):254-266, 1981.

The effects of continuous microperfusion of the visual cortex with either norepinephrine (NE) or 6-hydroxydopamine (6-OHDA) were studied in young kittens that had been monocularly deprived at 4 weeks of age for a week and then allowed to use both eyes for various times after reopening of the closed eyelid. The time course of recovery of the normal ocular dominance distribution in these two experimental conditions was compared with that of control kittens that had similar visual experience. The recovery of binocular cortical cells from the effects of the brief monocular deprivation was accelerated by concomitant, continuous perfusion of NE, and largely delayed in the visual cortex that had been depleted of its catecholamine terminals by perfusion of 6-OHDA. 32 references. (Author abstract modified)

003025 Kasarskis, Edward J.; Karpiak, Stephen E.; Rapport, Maurice M.; Yu, Robert K.; Bass, Norman H. Dept. of Neurology, University of Kentucky, Albert B. Chandler Medical Center, Lexington, KY 40536 **Abnormal maturation of cerebral cortex and behavioral deficit in adult rats after neonatal administration of antibodies to ganglioside.** Developmental Brain Research. 1(1):25-35, 1981.

Abnormal maturation of the cerebral cortex and behavioral deficit in adult rats after neonatal administration of antibodies to ganglioside is described. Five-day-old rats received a single injection of antiserum to ganglioside into the cisterna magna and were compared to control animals injected with the antiserum which had been absorbed with pure GM1 ganglioside to remove the specific antibodies. Both groups showed normal rates of body growth. However, animals receiving antiganglioside serum had, at 60 days of age, impaired performance when tested on a complex learning task (DRL) as well as chemical and morphological alterations on the somatosensory cerebral cortex. Results suggest that antibodies to GM1 ganglioside interfere with optimal neonatal development of both dendrites and myelin in cerebaral cortex. Results provide an animal model in which an immunologically mediated disturbance of cortical development is associated with chronic behavioral impairment. 34 references. (Author abstract modified)

003026 Kavaliers, Martin; Hawkins, Mike F. Dept. of Zoology, University of Western Ontario, London, Ontario N6A 5B7, Canada **Bombesin alters behavioral thermoregulation in fish.** Life Sciences. 28(12):1361-1364, 1981.

Bombesin was microinjected into the ventricular system of a teleost fish, Catostomus commersoni, to evaluate its effects on behavioral thermoregulation in a horizontal thermal gradient. General locomotor activity was also examined. Results demonstrate that bombesin decreased the behaviorally selected internal body temperatures by 5 to 7 degrees C relative to controls and that the latency of the response was dose dependent. The peptide did not change locomotor activity. Results are discussed in relation to body temeprature setpoint(s) and possible implications for endotherm thermoregulation. 6 references. (Author abstract)

003027 Kawasaki, Kazuo; Matsushita, Akira. Division of Pharmacology, Shionogi Research Laboratories, Shionogi and Co., Ltd., Fukushima-ku, Osaka 553, Japan **Sensitive depressant effect of benzodiazepines on the crossed extensor reflex in chloralose-anesthetized rats.** Life Sciences. 28(12):1391-1398, 1981.

Benzodiazepine derivatives doses dependently depressed the crossed extensor reflex (CER) in the hind lib of chloralose anesthetized rats when administered in very small doses that did not cause any behavioral and electrophysiological changes in other reported tests. Only medazepam showed a characteristic biphasic inhibition, a transient and weak inhibition followed by a long lasting inhibition. The effects of benzodiazepines were clearly antagonized by a subconvulsive dose of bicuculline, but not by strychnine. The ED50 values of diazepam, estazolam, nitrazepam, medazepam, and chlordiazepoxide in inhibiting the CER very closely correlated with their documented potencies in displacing 3H-diazepam binding to rat brain benzodiazepine receptors. Results suggest that the CER inhibition by benzodiazepines is mediated by GABAergic transmission and the CER in chloralose anesthetized rat can be used as a favorable indicator to detect the action of BZ via interactions with benzodiazepine receptors in vivo. 23 references. (Author abstract modified)

003028 Keresztes-Nagy, Patricia; Rosenfeld, J. Peter. Rosenfeld: Dept. of Psychology, Cresap Neuroscience Laboratory, Northwestern University, Evanston, IL 60201 **Naloxone-reversible duplication by lanthanum of opiate analgesia effects on orofacial, lower body and central nociception.** Brain Research. 208(1):234-239, 1981.

Antagonisms of analgesia for tail flick and paw lick (hotplate) reactions in rats were examined using intracranially microinjected lanthanum (La3) in midbrain ventrolateral central gray. Also examined were La3 effects on orofacial pain (and its possible reversal by naloxone) and La3 effects on aversive dorsal midbrain stimulation. La3 induced responses were compared with characteristic opiate analgesia effects. The data extend earlier studies of La3 analgesia by demonstrating four new effects of central gray La3 microinjection previously reported with opiates: 1) profound effects on orofacial thermal nociception; 2) significant analgesic effects on tail flick and hotplate tests, which were nevertheless significantly smaller than effects on face rub tests; 3) no effect on aversive reaction threshold to midbrain stimulation (using a La3 dose effectively analgesic for peripheral nociception); and 4) total naloxone and Ca2 reversibility of all analgesia. 20 references.

003029 King, William Blackstone, Jr. University of California, Los Angeles **Long lasting effects of chronic administration of hallucinogenic drugs on rat social and emotional behavior. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3224-B, 1981. Ann Arbor, Univ. Microfilms No. 8104008, 107p., 1980.

To test the possibility that hallucinogens can produce experimentally demonstrable, long-lasting alterations in behavior, two experiments were done. In the first, rats received chronic LSD via a subcutaneously implanted delivery system which delivered a total of 80mcg LSD over 7 days or 80mcg LSD in seven equal daily injections or placebo. Thirty days after drug administration only the rats that had received continuous LSD showed long-lasting behavioral alterations, consisting of decreased exploratory behavior in a novel environment and increased social behavior. The second experiment was similar to the first except that rats received a total of 438mcg of 5-methoxy-N,N-dimethyltryptamine instead of the LSD. Behavioral alterations were found 30 days later in both the rats receiving the drug by daily injection and by continuous delivery. Both drug groups showed a decrease in defecation in the social open field; in addition, the injected rats showed an increase in acoustic startle response, while the rats which had received the drug by continuous administration showed an increase in reactivity to handling. Results indicate that chronic hallucinogen administration causes long lasting behavioral changes in rats, but that the nature of the changes depend both upon the drug and the mode of its administration. (Journal abstract modified)

003030 Korczynski, Renard; Fonberg, Elzbieta. Dept. of Neurophysiology, Nencki Institute of Experimental Biology, Pasteura 3, 02-093 Warsaw, Poland **The effects of imipramine treatment on the unconditioned alimentary behavior and classical conditioned salivary reactions in dogs.** Acta Neurobiologiae Experimentalis. 39(3):157-171, 1979.

The effects of imipramine on the unconditioned alimentary behavior and classical conditioned salivary reactions of dogs were investigated. Imipramine decreased both conditioned and unconditioned salivation, but only slightly decreased food intake. In most dogs, increase of general arousal and improvement of social contact was observed. Differentiation of conditioned salivation to CS and CS- was disturbed during imipramine treatment, due to the prominent decrease of conditioned salivary reflexes to CS and increase of reactions to CS-. It is concluded that in the evaluation of the effect of imipramine, one should take into consideration its differential influences on various motor, autonomic, and emotional components, and central and peripheral components of alimentary behaviors. Great intersubject variability was observed. 20 references. (Author abstract modified)

003031 Kovacs, Gabor L.; Szabo, Gyula; Penke, Botond; Telegdy, Gyula. Institute of Pathophysiology, University Medical School, Semmelweis u.1.P.O.B. 531, H-6701 Szeged, Hungary **Effects of cholecystokinin octapeptide on striatal dopamine metabolism and on apomorphine-induced stereotyped cage-climbing in mice.** European Journal of Pharmacology. 69(3):313-319, 1981.

The effects of sulfated and nonsulfated cholecystokinin octapeptide (CCK-8-SE and CCK-8-NS, respectively) on striatal dopamine (DA) metabolism were investigated in male CFLP mice. The disappearance of striatal DA after synthesis inhibition with alpha-methyl-p-tyrosine was facilitated by CCK-8-NS, but not by CCK-8-SE. Neither form of CCK-8 affected in vitro uptake of 3H-DA by striatal slices, but both increased potassium evoked release of 3H-DA from striatal slices. Apomorphine induced stereotyped cage climbing behavior was not affected by CCK-8-SE, but was enhanced by CCK-8-NS; this effect was antagonized by haloperidol, but not by naloxone. Results suggest that CCK-8-NS acts on central dopaminergic mechanisms. 26 references. (Author abstract modified)

003032 Kuribara, Hisashi; Tadokoro, Sakutaro. Div. for Behavior Analysis, Behavior Research Institute, School of Medicine, Gunma University, 3-39-22 Showa-machi, Maebashi 371, Japan **Correlation between antiavoidance activities of antipsychotic drugs in rats and daily clinical doses.** Pharmacology Biochemistry and Behavior. 14(2):181-192, 1981.

The effects of 28 antipsychotic drugs on two types of avoidance responses in rats (Sidman avoidance and discriminated avoidance) were investigated and compared with clinical effects of daily administration of these compounds. Almost all drugs except sulpiride and clozapine suppressed the avoidance responses with a dose dependent decrease in response rate and increase in shock rate in the Sidman avoidance performance or a decrease in both the response and avoidance rates in the discriminated avoidance task. In most cases the potencies of the avoidance suppressing effects of the drugs were well correlated with their clinical daily doses. Results suggest that the avoidance response in rats is applicable in evaluating the clinical efficacies of antipsychotic drugs. 44 references. (Author abstract modified)

003033 Kuruvilla, Alice; Uretsky, Norman J. Dept. of Pharmacology, Cristian Medical College, Vellore, S. India **Effect of sodium valproate on motor function regulated by the activation of GABA receptors.** Psychopharmacology. 72(2):167-172, 1981.

To determine whether GABA can play a functional role in the pharmacological effects of valproate, both valproate and GABA were injected directly into the nucleus accumbens and the substantia nigra, (in male Sprague-Dawley rats) and the effects of these compounds on motor function were studied. Both GABA and sodium valproate inhibited the hyperactivity induced by bilateral injection of dopamine into the nucleus accumbens. Pictrotoxin, a GABA antagonist, blocked the inhibitory effect of valproate. When injected into the pars reticulata of the substantia nigra, both sodium valproate and GABA enhanced apomorphine induced circling in rats with a unilateral lesion of the lateral hypothalamus caused by 6-hydroxydopamine. This effect was blocked by the systemic administration of picrotoxin. Results suggest that sodium valproate can produce effects that result from the activation of GABA receptor sites in the brain. 30 references. (Author abstract modified)

003034 Lahti, Robert A.; Barsuhn, Craig. Upjohn Co., Kalamazoo, MI 49001 **Benzodiazepines, stress and rat plasma corticosteroids: the role of indoleamines.** Research Communications in Psychology, Psychiatry and Behavior. 5(4):369-383, 1980.

Results are reported from studies into the mode of action of the benzodiazepines in preventing elevations in plasma corticosteroids as a result of an applied stress in rats. Studies utilizing elevations in plasma corticosteroids as an indicator of stress did not confirm the postulate that the benzodiazepines exert their anxiolytic activity by blocking serotonergic receptors. The effect of diazepam in blocking stress induced elevation was antagonized by 5-hydroxytryptophan pretreatment in a noncompetitive manner, but the corticosteroid elevating activity of the indoleamine alpha-ethyltryptamine could be reversed by diazepam, and this result was comparable to those described in other behavioral studies used to formulate the hypothesis. Thus it appears that the benzodiazepines exert their clinical effect via an indole system, and that the system is probably not serotonergic. The recent findings of a beta carboline in human urine, which inhibits benzediazepine receptor interactions) supports this view. 8 references. (Author abstract modified)

003035 Larue-Achagiotis, C.; Le Magnen, J. Lab. de Neurophysiologie Sensorielle et Comportementale, College de France, 11, place Marcelin Berthelot, F-75231 Paris Cedex 05, France **Metabolic correlates of the effects of 2-deoxy-D-glucose on meal size and post-meal satiety in rats.** Physiology & Behavior. 26(2):193-196, 1981.

The effects of 2-deoxy-D-glucose (2DG, 250mg/kg i.p.) on meal size and postmeal satiety were studied in male Wistar rats after 0 to 6 hours of food deprivation. In rats treated with 2-DG at night, the size of the first meal was reduced but the postmeal interval was not altered, compared to controls. The reduction in meal size was associated with high levels of plasma glucose (PG) and plasma free fatty acid (PFFA) after the meal or in the absence of food. In animals treated during the day, 2-DG reduced the latency to eat and the meal to meal interval without changing meal size. The acceleration of meal onsets was associated with higher PG and lower PFFA levels 30 minutes after the meal than at the corresponding time at night. 8 references. (Author abstract modified)

003036 Loscher, Wolfgang. Lab. f. Pharmakologie u. Toxikologie, Fachbereich Veterinarmedizin, Freie Universitat Koserstr. 20, D-1000 Berlin 33, West Germany **A comparative study of the pharmacology of inhibitors of GABA-metabolism.** Naunyn-Schmiedeberg's Archives of Pharmacology. 315(2):119-128, 1980.

The anticonvulsant, biochemical, and toxic effects of four catalytic inhibitors of GABA-transaminase (gabaculine, gamma-acetylenic-GABA, gamma-vinyl-GABA, and ethanolamine-O-sulphate) were compared with those aminooxyacetic acid (AOAA) and sodium valproate (VPA) in male NMRI mice. The effects of gabaculine, gamma-acetylenic-GABA, and gamma-vinyl-GABA were nonspecific. Gamma-acetylenic-GABA, gamma-vinyl-GABA, and ethanolamine-O-sulphate had only weak anticonvulsant potency. AOAA and gabaculine were toxic or lethal at anticonvulsant doses. VPA was the only drug tested that showed satisfactory anticonvulsant potency with relatively low toxicity. It is concluded that GABA-transaminase inhibitors are not suitable for treatment of convulsive disorders in humans, but may be useful tools for manipulating brain GABA levels in studies of experimental epilepsy. 50 references. (Author abstract modified)

003037 Luttinger, D.; Nemeroff, C. B.; Mason, G. A.; Frye, G. D.; Breese, G. R.; Prange, A. J., Jr. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Enhancement of ethanol-induced sedation and hypothermia by centrally administered neurotensin, beta-endorphin and bombesin.** Neuropharmacology. 20(3):305-309, 1981.

The duration of sedation induced by 5.2g/kg ethanol in male Swiss-Webster mice was potentiated by intracisternal administration of neurotensin, beta-endorphin, or bombesin. The enhancement of ethanol induced sedation was correlated with the potentiation of ethanol induced hypothermia for all three endogenous neuropeptides. Since no dose of the three neuropeptides administered alone produced loss of the righting reflex, it is concluded that the enhancement of ethanol induced sleep by the these neuropeptides is probably not due to the summation of sedative effects. None of the neuropeptides significantly altered blood or brain ethanol concentrations. 17 references. (Author abstract modified)

003038 Lyness, W. H.; Mycek, Mary J. Dept. of Pharmacology and Therapeutics, Texas Tech University, Lubbock, TX 79430 **Potentiation of barbiturate hypnosis by probenecid: differential effect in tolerant animals.** Neuropharmacology. 20(3):217-226, 1981.

Probenecid (200mg/kg i.p.) potentiated the hypnotic effect of intracerebroventricular (i.c.v.) phenobarbital and delayed the efflux of phenobarbital from the brains of male Sprague-Dawley rats. Probenecid was used to investigate whether acid transport participates in the elimination of i.c.v. phenobarbitol, with the expectation that this might increase the duration of loss of righting reflex. The duration of phenobarbital hypnosis increased from 14.4 to 26.4 min in naive rats and from 2.1 to 25.5 min in rats made tolerant to phenobarbital. The potentiation of phenobarbital hypnosis could not be attributed to the sedative effects of probenecid. Probenecid also prolonged hypnosis produced by i.c.v. injection of barbital or i.p. injection of hexobarbital, and did not decrease the metabolism of hexobarbital. 28 references. (Author abstract modified)

003039 Mares, P.; Schickerova, R. Institute of Physiology, CSAV, Videnska 1083, CS-142 20 Praha, Czechoslovakia **Seizures elicited by subcutaneous injection of metrazol during ontogenesis in rats.** Activitas Nervosa Superior. 22(4):264-268, 1980.

Metrazol administered subcutaneously at a dose of 8mg/kg was found to elicit genuine minimal seizures (predominantly clonic) in adult, 45-day-old rats and 25-day-old rats. The same dose of metrazol resulted in long-lasting generalized tonic/clonic seizures in rats aged 5 days and younger. Eighteen-day-old rats represented a transitory stage in which both types of seizures were present: minor seizures at first and then, after a short resting period, major seizures. The different seizure pattern in young rats was not induced by their higher sensitivity to metrazol, but was caused by the level of neural maturation. 14 references. (Author abstract modified)

003040 Maricq, Andres V.; Roberts, Seth; Church, Russell M. Church: Dept. of Psychology, Brown University, Providence, RI 02912 **Methamphetamine and time estimation.** Journal of Experimental Psychology: Animal Behavior Processes. 7(1):18-30, 1981.

The effect of methamphetamine on the performance of rats in two timing tasks was studied in three experiments. When food sometimes followed the first response after 20 seconds of a signal, the response rate increased to a peak near 20 seconds and then declined. Methamphetamine decreased the time of the peak. When one response (a short response) was reinforced following a short signal and a different response (long response) was reinforced following a long signal, the probability of a long response increased as a function of signal duration. (The short and long signals were 1 and 4, 2 and 8, or 4 and 16 seconds. The point of indifference (50% long response) occurred near the geometric mean of the extreme durations, and methamphetamine decreased the point of indifference by about 10%. The results suggest that methamphetamine icreases the speed of an internal clock used by rats in time discrimination tasks. 28 references. (Author abstract modified)

003041 Maroli, Allan Norman. University of Cincinnati **Influence of morphine on the discriminative stimulus properties of rewarding lateral hypothalamic stimulation. (Ph.D. dissertation).** Dissertation Abstract International. 41(7):2816-B, 1981. Ann Arbor, Univ. Microfilms No. 8029680, 56p., 1980.

Intensity related changes produced by morphine in the discriminative stimulus complex of rewarding lateral hypothalamic stimulation were assessed in male albino rats. Animals were capable of differentiating extremely small intensity changes of brain stimulation as a difference of 6 mua was sufficient to yield reliable discriminative responding. Morphine was found to alter the generalization gradient in an orderly way, producing a statistically significant increase in the incidence of responding on the low intensity appropriate level. At the time and drug dosage parameters employed morphine also yielded a statistically significant increase in self-stimulation rates. Results suggest that morphine may attenuate some intensive dimension of the discriminative stimulus complex of rewarding lateral hypothalamic stimulation. The possibility that morphine's characteristic facilitative effect on self-stimulation behavior may result from the suppression of an aversive concomitant of the brain stimulation is discussed. (Journal abstract modified)

003042 Martin, James R.; Overstreet, David H.; Driscoll, Peter; Battig, Karl. Behavioral Science Institute, Behavioral Biology Lab., Swiss Federal Institute of Technology, E.T.H.Z., CH-8092 Zurich, Switzerland **Effects of scopolamine, pilocarpine, and oxotremorine on the exploratory behavior of two psychogenetically selected lines of rats in a complex maze.** Psychopharmacology. 72(2):135-142, 1981.

Rats of two psychogenetically selected lines received pretest i.p. injections of scopolamine, pilocarpine, or oxotremorine and were subsequently placed in a complex enclosed maze of the Dashiell type that included a small, central, illuminated arena. Following vehicle injections, Roman high avoidance rats (RHA/Verh) were significantly more active, explored more maze sectors, and required less time to activate the initial 24 different photocells uniformly distributed throughout the maze than did Roman low avoidance rats (RLA/Verh). Results following drug administration suggest that the two rat strains are differentially sensitive to central cholinergic manipulation with the muscarinic receptor agonists pilocarpine and oxotremorine. The data demonstrate that manipulation of the central cholinergic system with scopolamine, pilocarpine, or oxotremorine, despite their different pharmacological mechanisms, impairs maze patrolling behavior. 43 references. (Author abstract modified)

003043 Martinez-Roldan, C.; Garrido-Garcia, J. Laboratorios MADE, S.A., Madrid, Spain /**Protective action of L-5-hydroxytryptophan L-glutamate (MADE-1932) during electroshock treatment (ECT)**./ Accion protectora del L-glutamato de L-5 hidroxitriptofano (MADE-1932) frente al electrochoque (TEC). Revista de Psiquiatria y Psicologia Medica de Europa etc. 14(5):59-68, 1980.

The protective action of L-5 hydroxytryptophan L-glutamate (MADE-1932) during electroshock treatment was studied. A sample of 40 rats was divided into four groups of 10 rats each. The first group (control) received a placebo, while the second, third, and fourth groups were administered 5, 10, and 20mg/kg of the drug, respectively. All four groups were then given electroshock in rising voltages (50 to 80). Results show that the control group presented clonic convulsions. The other groups were protected significantly from death and convulsions. This protective action of MADE-1932 demonstrates dose dependency. (Journal abstract modified)

003044 Masserano, Joseph M.; King, Carl. King: Dept. of Pharmacology, Louisiana State University, School of Medicine, 1542 Tulane Ave., New Orleans, LA 70112 **TRH increases locomotor activity in rats after injection into the hypothalamus.** European Journal of Pharmacology. 69(2):217-219, 1981.

Bilateral injections of thyrotropin releasing hormone (TRH, 2mcg) into the hypothalamus of male Sprague-Dawley rats increased locomotor activity. No increase in locomotor activity was seen after bilateral injections of TRH into the caudate nucleus or septum. 8 references. (Author abstract modified)

003045 Matthews, William D.; Intoccia, Alfred P.; Osborne, Virginia L.; McCafferty, Gerald P. Dept. of Pharmacology, F-60, Smith Kline and French Laboratories, Philadelphia, PA 19101 **Correlation of (14C)muscimol concentration in rat brain with anticonvulsant activity.** European Journal of Pharmacology. 69(3):249-254, 1981.

Brain levels of (14C)muscimol and anticonvulsant activity against bicuculline were studied in male Sprague-Dawley rats after i.v. injection of 0.25 to 2.0mg/kg labeled muscimol. Peak brain concentrations of (14C)muscimol and maximal protection against bicuculline induced seizures occurred simultaneously, 30 minutes after injection. The half-life for the disappearance of (14C)muscimol was 117 minutes, compared to a half-life of 119 minutes for the decrease in anticonvulsant activity. Results indicate that the labeled GABA agonist penetrates the brain rapidly after i.v. injection and that unchanged muscimol (rather than a metabolite) antagonizes seizures induced by the GABA antagonist bicuculline. 13 references. (Author abstract modified)

003046 McCleary, Philip E.; Leander, J. David. Leander: Dept. of Pharmacology, University of North Carolina, School of Medicine 231-H, Chapel Hill, NC 27514 **Clonidine analgesia and suppression of operant responding: dissociation of mechanism.** European Journal of Pharmacology. 69(1):63-69, 1981.

The effects of clonidine and xylazine on analgesia (tail withdrawal from hot water) and on operant responding maintained by a fixed-ratio 20 response schedule of food presentation were compared in male Long-Evans hooded rats. Clonidine (2 to 8mg/kg) produced dose dependent increases in tail withdrawal latency and was about twice as potent as xylazine (8 to 16mg/kg). Clonidine (0.0063 to 0.2mg/kg) and xylazine (0.25 to 8mg/kg) both produced dose dependent suppression of fixed-ratio responding, but clonidine was about 40 times more potent than xylazine. The interaction of clonidine with yohimbine, phenoxybenzamine, and nisoxetine indicated that clonidine exerts its effects on tail withdrawal latency and operant behavior through separate mechanisms. Stimulation of postsynaptic alpha-adrenoceptors appears to be a significant component of clonidine induced analgesia, whereas behavioral suppression appears to be mediated by presynaptic receptors on noradrenergic neurons or by adrenergic receptors. 25 references. (Author abstract modified)

003047 McGivney, William Thomas. University of North Carolina at Chapel Hill **A characterization of the behavioral effects of levo-alpha-acetylmethadol in the rat and in the pigeon. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):2995-B, 1981. Ann Arbor, Univ. Microfilms No. 8104409, 176p., 1980.

The effects of levo-alpha-acetylmethadol (LAAM) and its proposed active metabolites, levo-alpha-noracetylmethadol (N-LAAM) and levo-alpha-dinoracetylmethadol (DN-LAAM), on schedule controlled responding in the rat and in the pigeon were examined. LAAM's behavioral effects were compared with those observed after the administration of methadone. Results demonstrate that LAAM possessed many of the behavioral characteristics of the opioids. LAAM increases rates of responding under the fixed-interval component in both the rat and the pigeon, while, at higher doses, it decreases rates of responding under both fixed-interval and fixed-ratio components. Tolerance developed in the rate decreasing effects of LAAM, and physical dependence was produced by the chronic administration of LAAM in the rat. Oral LAAM was about twofold more potent in producing alterations in schedule controlled behavior than oral methadone in the rat, while in the pigeon, the two drugs were equipotent. LAAM's behavioral effects were characterized by a longer duration of action than those of methadone. The suggestion that LAAM's effects are attributable to its metabolic conversion to more active compounds was evaluated. The potency and duration of action of these metabolites suggest that they contribute importantly to the behavioral effects observed after the administration of the parent compound. (Journal abstract modified)

003048 McGlone, John J.; Kelley, Keith W.; Gaskins, Charles T. Dept. of Animal Science, Washington State University, Pullman, WA 99164 **Lithium and porcine aggression.** Journal of Animal Science. 51(2):447-455, 1981.

One hundred and forty eight growing pigs were used in four experiments conducted to determine the effect of lithium (Li) on the level of aggression among newly mixed, previously unacquainted pigs. Pigs maintained on low levels of dietary Li attained serum Li concentrations of .1mEq/liter to .7mEq/liter. At these low serum levels, biting activity was consistently lower than it was among control pigs, although the difference was usually not statistically significant. Low levels of dietary Li did not significantly affect the rate of gain or feed efficiency. When high concentrations of serum Li were achieved by an intraperitoneal injection, pig aggression was reduced to almost zero for 10 hours postmixing. This effect probably is due to drug induced malaise associated with potentially toxic serum Li concentrations. These data suggest that Li can substantially reduce aggression among pigs that are unfamiliar with each other. 27 references. (Author abstract modified)

003049 Merkel, A. D.; Wayner, M. J.; Jolicoeur, F. B.; Mintz, R. Wayner: Brain Research Lab., Syracuse University, 601 University Ave., Syracuse, NY 13210 **Effects of caffeine administration on food and water consumption under various experimental conditions.** Pharmacology Biochemistry and Behavior. 14(2):235-240, 1981.

The effects of caffeine on food and water intake were assessed in rats maintained under several experimental conditions. In Experiment 1, caffeine, was injected into 23 hour food deprived Ss, 23 hour water deprived Ss, or ad lib feeding and drinking Ss. In Experiment 2, animals were adapted to a 21 hour food deprivation schedule and administered the same doses of caffeine as were used in Experiment 1. Results indicate that caffeine both enhances and decreases food and water intake and that the effects observed depend on the experimental circumstances. 27 references. (Author abstract modified)

003050 Meszaros, J.; Tarchalska, B.; Gajewska, S.; Janicki, P.; Duriasz, H.; Szreniawski, Z. Dept. of Pharmacology, Institute of Physiological Sciences, Warsaw Medical Academy, 00-927 Warsaw, Poland **Substance P, hexapeptide pGlu6(SP6-11), analgesia and serotonin depletion.** Pharmacology Biochemistry and Behavior. 14(1):11-15, 1981.

Substance-P had marked analgesic activity after intraventricular administration in male Wistar rats and after i.p. injection in male Swiss mice. The hexapeptide pGlu6(SP6-11) had analgesic effects in mice but not in rats. Depletion of serotonin with p-chlorophenylalanine abolished the antinociceptive activity in mice, but not in rats. Lesion of the raphe nuclei blocked the activity of substance-P in rats. Results suggest that serotonergic mechanisms may be more important in pain control in mice than in rats. 11 references. (Author abstract modified)

003051 Micheau, Jacques; Destrade, Claude; Soumireu-Mourat, Bernard. Soumireu-Mourat: Laboratoire de Neurobiologie des Comportements Universite de Provence, F-13397 Marseille Cedex 13, France **Intraventricular corticosterone injection facilitates memory of an appetitive discriminative task in mice.** Behavioral and Neural Biology. 31(1):100-104, 1981.

The effect of 1.0mcg of corticosterone on memory consolidation of two appetitive tasks was examined in mice. The immediate posttraining injection into the cerebral ventricles did not affect memory consolidation of a continuously reinforced operant condition task. Using a discriminative operant conditioning procedure with the same Skinner box, this treatment facilitated retention. These results suggest that memory consolidation of adaptive behaviors can be modulated through interaction between central nervous structures and the pituitary adrenal axis. 5 references. (Author abstract modified)

003052 Miczek, Klaus A. Tufts University, Medford, MA 02115 **Pharmacological evidence for catecholamine involvement in animal aggression.** Psychopharmacology Bulletin. 17(1):60-62, 1981.

Pharmacological evidence for catecholamine involvement in animal aggression is reviewed. Studies indicate that pharmacological manipulations of brain catecholamies can have profound, mostly disruptive, effects on attack and threat behavior; comparable changes are seen in defensive and flight reactions as well as affiliative behavior. The primary behavioral change due to catecholamine manipulations seem to depend mainly on the situational and social context. Recent studies in mice, rats, and squirrel monkeys suggest a modulating rather than a critical role for catechol in mechanisms regulating agonistic behavior. 12 references. (Author abstract modified)

003053 Miksic, Stephen; Sherman, Gary; Lal, Harbans. 7121 Thomas Boulevard, Pittsburgh, PA 15208 **Discriminative response control by naloxone in morphine pretreated rats.** Psychopharmacology. 72(2):179-184, 1981.

Twelve male hooded rats were trained to discriminate naloxone from saline injections in a operant procedure using a lever-press response. On certain days, according to a counterbalanced training schedule, naloxone was administered 8 hours after 40mg/kg morphine and 10 minutes prior to a trial in which food was available on a FR10 schedule from one of two levers in a dual lever operant chamber. On other days, saline was administered 10 minutes prior to a trial in which food was made available by pressing the other lever. After criterion performance for acquisition of the discrimination had been reached, the nature of the discrimination was studied. Discrimination of naloxone was dose dependent and was significantly diminished when naloxone was administered 36 hours after morphine. Partial generalization of cyclazocine with naloxone was observed. Spontaneous withdrawal from morphine, tested during trials preceded by an injection of saline instead of naloxone at various time intervals after morphine, did not generalize with the naloxone discriminative stimulus. 18 references. (Author abstract modified)

003054 Miley, William M.; Frank, Michael; Hoxter, A. Lee. Richard Stockton State College, Pomona, NJ 08240 **Rat-pup killing and maternal behavior in male Long-Evans rats: prenatal stimulation and postnatal testosterone.** Bulletin of the Psychonomic Society. 17(2):119-122, 1981.

The effects of prenatal stimulation and postnatal testosterone administration on rat pup killing and maternal behavior of male Long-Evans rats were investigated. During each of the last 5 days of pregnancy, Long-Evans rats received one of the following conditions: 45 minutes of restraint and intense illumination, 3 minutes of handling, 3 minutes of restraint and .1mg of androstenedione, and 3 minutes of restraint and .1ml sesame oil. Half of the offspring of each group received testosterone postnatally. In adulthood, the handled group's offspring killed many pups with or without exogenous testosterone; the other offspring killed many only with testosterone. More animals that received androstenedione prenatally and testosterone postnatally killed pups than animals that receive either oil or 45 minutes of restraint and intense illumination prenatally and testosterone postnatally. Subsequent studies showed that fewer prenatally unhandled animals killed than prenatally handled animals. These prenatally unhandled animals required less time to retrieve pups (and more of them did so) than did any of the other groups. 15 references. (Author abstract modified)

003055 Miller, Van; Domjan, Michael. Dept. of Psychology, University of Texas, Austin, TX 78712 **Selective sensitization induced by lithium malaise and footshock in rats.** Behavioral and Neural Biology. 31(1):42-55, 1981.

In a study of response sensitization, Sprague-Dawley rats were allowed to chose between a novel and a familiar stimulus presented contingent upon licking a drinking spout after having been exposed to an aversive stimulus. Rats pretreated with footshock showed reduced preference for a novel stimulus if shock was administered immediately before the test session, but not if shock occurred 5 or 25 minutes earlier (Experiment 1). Subjects pretreated with lithium chloride (LiCl) before a choice test between a novel saccharin solution and familiar tap water showed a reduced preference for saccharin if the LiCl was administered 35 minutes before testing, but not if the LiCl was administered 6 hours earlier (Experiment 2). However, pretreatment with LiCl did not reduce subjects' preference for a novel saccharin solution (Experiment 3). This demonstration of selective sensitization effects is contrary to characterizations of sensitization as a general, nonspecific mechanism. The results are disucssed in terms of anatomically mediated differential processing of interoceptive and exteroceptive stimuli. 25 references. (Author abstract)

003056 Mirmiran, M.; Van de Poll, N. E.; Corner, M. A.; van Oyen, H. G.; Bour, H. L. Netherlands Institute for Brain Research, IJdijk 28, 1095 KJ Amsterdam, The Netherlands **Suppression of active sleep by chronic treatment with chlorimipramine during early postnatal development: effects upon adult sleep and behavior in the rat.** Brain Research. 204(1):129-146, 1981.

To study the possible role of active sleep (physiologically equivalent to REM sleep) in brain development, male rats were injected twice daily with chlorimipramine, a potent monoamine reuptake blocker, from 1 week to 3 weeks of postnatal age. Active sleep was reduced to less than 10% of total sleep time, the level found in mature rats. In adulthood, the active sleep deprived rats showed a higher percentage of active sleep than did the control Ss, due to an increase in frequency and duration of active sleep epochs. The chlorimipramine treated rats also showed behavioral abnormalities in later life. These results demonstrate that early interference with the functioning of monoaminergic systems can have long lasting physiological and behavioral consequences. Furthermore, they are consistent with the hypothesis that AS is an important factor in normal brain development. 49 references. (Author abstract modified)

003057 Miyamoto, M.; Fukuda, N.; Narumi, S.; Nagai, Y.; Saji, Y.; Nagawa, Y. Central Research Division, Takeda Chemical Industries Ltd., Yodogawa-ku, Juso-Honmachi, Osaka 532, Japan **Gamma-butyrolactone-gamma-carbonyl-histidyl-prolinamide citrate (DN-1417): a novel TRH analog with potent effects on the central nervous system.** Life Sciences. 28(8):861-869, 1981.

A novel thyrotropin releasing hormone (TRH) analog, gamma-butyrolactone-gamma-carbonyl-histidyl-prolinamide citrate (DN-1417) with very low thyrotropin releasing activity was found to markedly increase motor activity in mice, with and without reserpine administration. DN-1417 also promoted arousal from pentobarbital or ethanol sleep and from loss of consciousness induced by concussive head injury, and reversed hypothermia induced by pentobarbital and reserpine. Circling behavior was provoked by comparatively low doses of DN-1417 in mice with unilateral striatal lesions, and the effect was prevented by pimozide and alpha-methyl-p-tyrosine. The results indicate that DN-1417 is more potent and longer acting than TRH in the CNS behavioral paradigms, and that some of the effects may be relevant to central monoaminergic systems. 30 references. (Author abstract)

003058 Mogilnicka, Ewa; Przewlocka, Barbara. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Cracow, Poland **Facilitated shock-induced aggression after chronic treatment with antidepressant drugs in the rat.** Pharmacology Biochemistry and Behavior. 14(2):129-132, 1981.

The effects of four antidepressant drugs with different mechanisms of action on shock induced fighting between pairs of rats were determined. Amitriptyline, imipramine, mianserin, and iprindole, given chronically, facilitated fighting behavior. Results with the apomorphine induced aggression model point to an increased function of the noradrenergic system, evoked by a chronic treatment with antidepressants. It is unlikely that the facilitation of shock induced fighting resulted from changes in the dopamine (DA) system, since the chronically administered antidepressants did not affect apomorphine stereotypy. 19 references. (Author abstract modified)

003059 Morley, John E.; Levine, Allen S. Levine: Neuroendocrine Research Lab., V.A. Medical Center, Minneapolis, MN 55417 **Bombesin inhibits stress-induced eating.** Pharmacology Biochemistry and Behavior. 14(2):149-151, 1981.

The effects of centrally administered bombesin, a tetradecapeptide originally isolated from amphibian skin, on short-term appetite regulation were investigated in rats using the Antelman mild tail pinch paradigm. Bombesin administered both intracerebroventricularly and parenterally suppressed stress induced eating in the rat. Intraventricular administration of bombesin resulted in hyperglycemia, which was abolished by adrenalectomy. It was found that the satiety inducing effect of bombesin was independent of the hyperglycemia it produces since suppression of stress induced eating was still present in adrenalectomized animals. 25 references. (Author abstract modified)

003060 Myslobodsky, M. S.; Golovchinsky, V.; Mintz, M. Psychobiology Research Unit, Tel Aviv University, Shareu 109, Ramat Aviv, Israel **Ketamine: convulsant or anti-convulsant?** Pharmacology Biochemistry and Behavior. 14(1):27-33, 1981.

Doses of ketamine that produce narcotic/cataleptic effects (50 to 100mg/kg i.p.) reduced the intensity of picrotoxin convulsions and eliminated seizures induced by metrazol in male Sprague-Dawley rats. Subcataleptic doses of ketamine (5 to 20mg/kg) increased the duration of mitigated convulsive symptoms (abortive grand mal fits and jerks), especially those evoked by picrotoxin. Narcoleptic/cataleptic doses of ketamine considerably increased the duration of the period of single jerks and multiple jerks after picrotoxin. Picrotoxin and metrazol transformed 1 to 2Hz ketamine complexes into 2 to 4Hz wave/spike discharges alternating with periods of suppressed electrocortical activity. Grand mal EEG patterns were typically dissociated from behavioral manifestations under 50 to 100mg/kg ketamine. 22 references. (Author abstract modified)

003061 Myslobodsky, Michael S.; Braun, Hava. Psychobiology Research Unit, Dept. of Psychology, Meir Hospital, Tel-Aviv University, Tel-Aviv, Israel **Does postural asymmetry indicate directionality of rotation in rats: role of sex and handling.** Behavioural Brain Research. 2(1):113-117, 1981.

The effects of amphetamine on postural asymmetry of male and female Wistar rats was assessed during four tests: 1) tail suspension; 2) tail holding; 3) tail pinch; and 4) walking on a narrow path. The tests were conducted prior to and following ()k-amphetamine administration. Rotational directionality was assessed in a rotometer. Only in female rats did postural adjustment during the tail pinch predict the direction of circling prior to and after amphetamine. In both surgically castrated and conjugated estrogen treated male rats, and in sham castrated and handled males, the tail pinch test caused the same dominant directionality as rotation under amphetamine. The duplicity of postural tests suggests that there is a multitude of systems controlling and modulating postural response. 14 references. (Author abstract modified)

003062 Neil, A.; Terenius, L. Dept. of Pharmacology, University of Uppsala, Box 573, S-751 23 Uppsala, Sweden **d-Propoxyphene acts differently from morphine on opioid receptor-effector mechanisms.** European Journal of Pharmacology. 69(1):33-39, 1981.

The receptor binding selectivity and antinociceptive effects of d-propoxyphene and morphine were compared. In binding studies in female Sprague-Dawley rat brain synaptosomes with dihydromorphine, naloxone, and an enkephalin analogue as radioactive ligands, d-propoxyphene differed from morphine in having a higher relative affinity for sites occupied by the peptide. In the hot plate test in male NMRI mice, naloxone was more effective in antagonizing antinociception induced by morphine than that induced by d-propoxyphene. The antinociceptive potency of d-propoxyphene was not attenuated in morphine tolerant mice. Results suggest that d-propoxyphene and morphine have different receptor/effector mechanisms. 24 references. (Author abstract modified)

003063 Noll, Katherine Lenorah McManus. Northern Illinois University **A test of a neurotransmitter model of the affective disorders. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3191-B, 1981. Ann Arbor, Univ. Microfilms No. 8101454, 198p., 1980.

A model of neurotransmitter relationships in the brain systems mediating motivation, and involving serotonin (5-HT), acetylcholine (ACh), dopamine (DA), and norepinephrine (NE), was tested with Long-Evans hooded rats in a learned helplessness model of depression. Shuttle box response deficits, relative to control values, were observed in groups treated with drugs to represent several of the postulated patterns of neurotransmitter alteration in the affective disorders. The greatest increase in escape latency was observed in the group pretreated with shock and drug treated to elevate ACh function and reduce 5-HT function; this pattern was postulated to represent the Bipolar-II group of affective disorder patients, who are most likely to attempt or commit suicide. Differences in escape latency were independent of the effects of the drugs on footshock sensitivity, but footshock sensitivity was altered by manipulation of 5-HT. Serotonin altering drugs reduced brain 5-HT levels by 50% or elevated by 400%. The results support the postulated patterns of neurotransmitter alteration in the affective disorders. (Journal abstract modified)

003064 Parrott, R. F.; Baldwin, B. A. ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Operant feeding and drinking in pigs following intracerebroventricular injection of synthetic cholecystokinin octapeptide.** Physiology & Behavior. 26(3):419-422, 1981.

Operant feeding and drinking was investigated in food deprived or water deprived pigs following intracerebroventricular (ICV) injection of a saline solution containing synthetic cholecystokinin (CCK) octapeptide. In 17 hour food deprived animals treated with 0, 5, 10, 20, or 40 units ICV, posttreatment food intake was significantly reduced in a dose related manner but drinking was unaffected. In 22 hour water deprived pigs treated with 0, 10, or 40 units CCK octapeptide ICV, no effect on drinking was apparent. Pigs injected intravenously with 40 units following 17 hours food deprivation did not reduce their food intake. 17 references. (Author abstract)

003065 Pepeu, G.; Gori, G.; Bartolini, L. Dept. of Pharmacology, Univeristy of Florence, Florence, Italy **Pharmacologic and therapeutic perspectives on dementia: an experimental approach.** In: Amaducci, L., Aging of the brain and dementia, vol. 13. New York, Raven, 1980. 326 p. (p. 271-274).

The few experimental animal models for investigating drugs used in treating senile dementia are briefly examined. Available drugs for this purpose are to date unsatisfactory, partly because of the lack of reliable animal models on which to carry out preclinical screening. The models that are currently in use include studies of neurochemical changes in senile animals, the injection of aluminum salt solutions into the intracranial area of cats, graded hypoxia, the analysis of degeneration of the dopaminergic pathways in the CNS via electrocoagulation or intranigral injection of 6-hydroxydopamine, and the administration of anticholinergic drugs. The most useful and simple approach involves pretreatment with anticholinergic drugs and evaluation of the insuing disruption of spontaneous or learned behavior. 21 references.

003066 Perry, William; Esposito, Ralph U.; Kornetsky, Conan. Kornetsky: Lab. of Behavioral Pharmacology, L-602, Boston University School of Medicine, 80 East Concord St., Boston, MA 02118 **Effects of chronic naloxone treatment on brain-stimulation reward.** Pharmacology Biochemistry and Behavior. 14(2):247-249, 1981.

Rats were tested on a rate free psychophysical procedure to determine the absolute reinforcement thresholds for self-stimulation behavior and the effects of naloxone on reward thresholds. Administration of naloxone for 5 days failed to alter the reinforcement thresholds obtained with this procedure. To the extent that naloxone is an effective antagonist of endogenous opioids, it is concluded that central endorphin systems are not necessary to support self-stimulation behavior. 24 references. (Author abstract modified)

003067 Post, Robert M.; Squillace, Kathleen M.; Pert, Agu; Sass, Willard. Section on Psychobiology, NIMH, Bldg. 10, Rm. 3S239, 900 Rockville Pike, Bethesda, MD 20205 **The effect of amygdala kindling on spontaneous and cocaine-induced motor activity and lidocaine seizures.** Psychopharmacology. 72(2):189-196, 1981.

Interactions of amygdala kindling and drug effects were explored in two experiments. Pretreatment of rats with cocaine for 10 days did not significantly affect the rate of amygdala kindling compared to saline or nonkindled control Ss. In contrast, daily amygdala kindling with 200mcA for 20 days substantially altered subsequent behavioral responses in a long-lasting fashion. Animals showed decreased spontaneous vertical rearing activity, as well as decreased cocaine induced vertical activity. In contrast, they were more reactive to the direct dopamine receptor agonist apomorphine. Eighteen days following completion of amygdala kindling, kindled animals were more sensitive to lidocaine induced convulsions; 88% of kindled animals, but only 24% of the implanted, sham stimulated control Ss, had seizures. These data suggest that amygdala kindling may produce long-lasting changes in selected spontaneous and drug induced behaviors, as well as in convulsive thresholds. Possible physiological and neurological changes underlying this altered responsivity are discussed. 56 references. (Author abstract modified)

003068 Quock, Raymond M.; Lucas, Thomas Scott. Division of Pharmacology, Dept. of Basic Sciences, Marquette University School of Dentistry, Milwaukee, WI 53233 **Enhancement of apomorphine-induced climbing in mice by reversible and irreversible narcotic antagonist drugs.** Life Sciences. 28(12):1421-1424, 1981.

The enhancement of apomorphine induced climbing in mice by reversible and irreversible narcotic antagonist drugs is described. Apomorphine produced a characteristic climbing syndrome in mice. Pretreatment of mice with increasing doses of the reversible narcotic antagonist naloxone resulted in a dose related enhancement of this activity. Central microinjection of mice with the irreversible narcotic antagonist drug chlornaltrexamine also resulted in significant potentiation of apomorphine induced climbing for up to 14 days following pretreatment. These data indicate that narcotic antagonist drugs of both reversible and irreversible types are capable of enhancing this dopaminergic drug effect in mice. 25 references. (Author abstract modified)

003069 Reinstein, Daniel Kendig. State University of New York at Binghamton **Behavioral and biochemical changes after hippocampal damage. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2820-B, 1981. Ann Arbor, Univ. Microfilms No. 8101563, 144p., 1980.

Rats with hippocampal, cortical, or sham control lesions were observed under two conditions at 7, 14, and 28 days after surgery. Animals were observed in an open field hole poke apparatus on measures of locomotion, rearing, grooming, and exploration. Animals were then injected unilaterally with saline or 3,4-dihydroxyphenylamino-2-imidazoline (DPI) into n. accumbens and observed in a rotation apparatus on measures of rotation, rearing, and grooming. In a third experiment, dopamine (DA) receptor binding was examined at the same postoperative times. Changes in locomotion, exploration, rearing, and grooming were observed at various postoperative times and each demonstrated a unique pattern of change consistent with previous findings. Treatment with DPI tended to normalize the behavior of hippocampally lesioned animals on a number of behaviors observed in the rotation apparatus. The receptor binding data suggests that much of the change in responsiveness to DPI may be related to changes in DA receptor sensitivity or receptor populations. Results are discussed in reference to the effects of hippocampal lesion on dimensions of response initiation and maintenance. (Journal abstract modified)

003070 Rekhtman, M. B.; Samsonova, N. A.; Kryzhanovskiy, G. N. Institut obshchey patologii i patologicheskoy fiziologii, AMN SSSR, Moskva, USSR **/Electrical activity and Na, K-ATPase level in the penicillin induced epileptogenic focus of the rat brain cortex, and the effect of diazepam./** Elektricheskaya aktivnost' i uroven' Na, K-ATFazy v epilepticheskom ochage, obrazovannom deystviyem penitsillina na kory gplovnogo mozga krys, i vliyaniye na nikh diazepama. Neyrofiziologiya. 12(4):349-357, 1980.

Electrical activity and Na, K-ATPase level in the penicillin induced epileptogenic focus of the rat cerebral cortex, and the effect of diazepam were studied in 70 white male rats. Silver ball electrodes were placed 0.5mm from the cortex. Penicillin application to the brain motor cortex resulted in the appearance of interictal discharges and seizures. Following the intramuscular injection of diazepam (2mg/kg) there was a 100% increase in the Na, K-ATPase activity of neuronal membranes in the epileptogenic focus. Interictal discharges and seizures changed in different ways after injection of diazepam. Results suggest that the differential effects of diazepam on seizures and interictal discharges may reflect different mechanisms of action with respect to electrical activity and Na, K-ATPase level. 37 references. (Journal abstract modified)

003071 Rick, J. T.; Gregson, A. N.; Leibowitz, S.; Adinolfi, M. Adinolfi: Pediatric Research Unit, Guy's Hospital Medical School, London SE1 9RT, England **Behavioural changes in adult rats following administration of antibodies against brain gangliosides.** Developmental Medicine and Child Neurology. 22(6):719-724, 1980.

Mature rats, previously trained in a standard two lever chamber, were injected with antibodies against gangliosides and the effect was evaluated in a series of different behavioral tests.

Compared with control Ss, the injected rats showed transient differences in their response to stimuli. The apparent counterintuitive superiority of the treated animals over the control Ss is discussed with reference to other experimental studies of young rats and to discrete pathological human conditions associated with the presence of brain antibodies. 19 references. (Author abstract)

003072 Ridley, R. M.; Haystead, T. A. J.; Baker, H. F. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, Middlesex, England **An involvement of dopamine in higher order choice mechanisms in the monkey.** Psychopharmacology. 72(2):173-177, 1981.

The involvement of dopamine in higher order choice mechanisms in the monkey was investigated. Low doses of amphetamine were found to induce choice perseveration in an object discrimination task under conditions where such perseveration either increases or decreases the number of rewards obtained as compared to chance performance. Neither stereotyped motor actions nor repetitive choice of position contributed to this effect, which could be blocked by pretreatment with the neuroleptic haloperidol. These results demonstrate that higher order choice mechanisms may involve dopamine systems in the primate. 23 references. (Author abstract modified)

003073 Rodgers, R. J.; Deacon, R. M. J. Postgraduate School of Psychology, University of Bradford, Bradford, England **Footshock-analgesia: prevention by behavioural manipulation but not by naloxone.** Physiology & Behavior. 26(2):183-187, 1981.

The effects of naloxone and behavioral manipulation on footshock analgesia were investigated in male Sprague-Dawley rats. Acute exposure to footshock significantly elevated tail flick latencies in single rats, but none in paired animals, which fought in response to shock. Naloxone hydrochloride (5mg/kg) failed to prevent the shock induced increases in latencies in unpaired animals. Results suggest that naloxone sensitive opiate receptors are not involved in footshock analgesia. 34 references. (Author abstract modified)

003074 Rodriguez-Sierra, Jorge F.; Terasawa, Ei; Goldfoot, David A.; DeWied, David. Terasawa: Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, WI 53706 **Testosterone potentiation of the effectiveness of ACTH1-24 on the induction of the stretch-yawning syndrome (SYS) in male guinea pigs.** Hormones and Behavior. 15(1):77-85, 1981.

Similarities and differences of response of the guinea-pig to intracranial ACTH was examined and compared to those reported for other species. Ventricular administration of ACTH1-24 stimulated stretch/yawning in a dose related manner. Daily subcutaneous treatment with testosterone propionate (TP) facilitated the effects of ACTH1-24 on this response. TP given without ACTH1-24 stimulated yawning but did not stimulate stretching or combined stretch/yawning. Unlike most other species, guinea-pigs did not display autogrooming, scratching, or wet dog shaking in response to intracranial ACTH1-24. The results suggest that testosterone may alter the sensitivity of neural mechanisms which are responsive to ACTH1-24. 122 references. (Author abstract modified)

003075 Rotiroti, D.; Naccari, F.; Ammendola, D.; De Gori, N.; Nistico, G. O. Institute of Pharmacology, Faculty of Medicine, University of Messina, Messina, Italy **Central effects of substance P in fowls.** Research Communications in Psychology, Psychiatry and Behavior. 5(4):397-406, 1980.

In adult fowls (Gallus domesticus) with cannulae chronically implanted by means of a stereotactic instrument into the cerebral ventricle or into selected areas of the brain, the effects of undecapeptide substance P(SP) given by these routes on behavior, electrocortical activity and body temperature were studied. SP infused into the cerebral ventricles produced an intense pattern of stereotyped movements lasting about 60 minutes, accompanied mostly by slow-wave sleep except after the highest doses used when an initial period of behavioral alertness and vocalization was observed. Body temperature increased only after the largest doses. Microinjection of SP into the n. mesencephalicus profundus (homologous to the mammalian s. nigra) also produced stereotyped movements which were superimposed on a tonic head/neck contralateral deviation. A similar pattern occurred after infusion into the hypothalamus. Pretreatment with haloperidol prevented stereotyped behavior elicited by SP infusion into the ventricles or into the n. mesencephalicus profundus, suggesting that such stereotyped movements are mediated through activation of dopaminergic mechanisms. 24 references. (Author abstract modified)

003076 Rudeen, P. Kevin; Symmes, Sandra K. Dept. of Anatomy, Bowman Gray School of Medicine, Winston-Salem, NC 27103 **Pineal gland and melatonin influence on chronic alcohol consumption by hamsters.** Pharmacology Biochemistry and Behavior. 14(2):143-147, 1981.

Pineal gland and melatonin influences on chronic alcohol consumption by hamsters were investigated. Melatonin, a pineal hormone, was administered either daily for 11 weeks as a subcutaneous injection or weekly as a subcutaneous beeswax implant for 5 weeks to hamsters allowed a free choice between water or a 10% ethanol solution. Food, water, and alcohol consumptions were measured on a daily basis. Animals treated by daily injection with melatonin consumed slightly less ethanol than animals not given melatonin. In light deprived animals given chronic implants of melatonin, alcohol consumption was reduced when compared to alcohol consumption by light deprived hamsters not receiving melatonin. Melatonin treatment also resulted in reducing daily total fluid intake as well as ethanol consumption in light deprived hamsters. The results indicate that the pineal gland may influence fluid consumption in the hamster, and indirectly alters the propensity of the hamster to consume alcohol. 15 references. (Author abstract modified)

003077 Sachs, Benjamin D.; Valcourt, Richard J.; Flagg, Henry C. Dept. of Psychology, U-20, University of Connecticut, Storrs, CT 06268 **Copulatory behavior and sexual reflexes of male rats treated with naloxone.** Pharmacology Biochemistry and Behavior. 14(2):251-253, 1981.

The effects of naloxone on copulatory behavior and sexual reflexes of male rats were investigated and a potential role for endogenous opiates in the regulation of sexual behavior of male rats was explored. Animals were injected with 15 to 45mg/kg naloxone hydrochloride 30 minutes prior to the start of reflex testing, and with 7.5 to 45mg/kg naloxone hydrochloride 30 minutes before testing for copulation. Naloxone resulted in a small but reliable decrease in the number of penile flips. Reflex latency and other measures of penile reflexes were unaffected. At all doses used, naloxone significantly prolonged the postejaculatory refractory period, with no other effects on copulation. 29 references. (Author abstract modified)

003078 Salles, K. S. S.; Colasanti, B. K.; Craig, C. R. Dept. of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Cyclic AMP-induced changes in the electroencephalogram and in behavior during morphine dependence and abstinence in the rat.** Sleep. 1:247-257, 1979.

Rats were prepared with permanent electrodes for recording activities of the electroencephalogram (EEG) and electromyogram (EMG) and were made morphine dependent by subcutaneous implantation. Abstinence was precipitated by removal of morphine pellets 72 hours later. During the first 2 days after pellet implantation, high voltage slow activity appeared in the EEG during behavioral wakefulness and stupor, while sleep and REM sleep were reduced greatly. By the third day, tolerance to these effects developed. After pellet removal, REM sleep time during the first day was reduced. Wet dog shake activity reached a maximum during the second day of abstinence. Treatment of a second group of rats with cyclic adenosine 3',5'-monophosphate (cAMP), 50mg/kg intraperitoneally once daily prior to and during induction of morphine dependence and during withdrawal, markedly reduced the appearance of morphine induced high voltage EEG slow activity after implantation of pellets. Behavioral arousal during the first 2 days after pellet implantation, on the other hand, was increased. After removal of pellets, from the cAMP treated rats sleep episodes occurred less frequently during the first day than in the control data. The incidence of wet shakes at this time was elevated. These results provide direct evidence for the involvement of brain cAMP in the medation of the central effects of morphine. (Journal abstract modified)

003079 Sanderson, C. A.; Rogers, L. J. Pharmacology Dept., Monash University, Clayton, 3168, Victoria, Australia **2,4,5-Trichlorophenoxyacetic acid causes behavioral effects in chickens at environmentally relevant doses.** Science. 211(4482):593-595, 1981.

Administration of the herbicide 2,4,5-trichlorophenoxyacetic acid to incubating chicken eggs altered behavior after hatching. Single doses, with no morphological effects, retarded learning (lowest dose, 7 milligrams per kilogram of bodyweight) and increased general activity (27 milligrams per kilogram) and jumping (13 milligrams per kilogram). Day 15 of incubation was the most susceptible stage of development. 10 references. (Author abstract)

003080 Sanger, D. J.; McCarthy, P. S.; Metcalf, G. Dept. of Pharmacology, Pharmaceutical Division, Reckitt and Colman, Dansom Lane, Hull HU8 7DS, England **The effects of opiate antagonists on food intake are stereospecific.** Neuropharmacology. 20(1):45-47, 1981.

The effects of the opiate antagonists naloxone, Mr1452/3 and Mr2266/7 on food intake of food deprived rats were investigated. A wide range of doses of naloxone was found to reduce food intake of food deprived rats, and this effect was found to have a relatively short duration of action. Similar reductions in eating were found with two benzomorphan compounds (Mr1452 and Mr2266) known to act as opiate antagonists. However, the () isomers of these compounds (Mr1453 and Mr2267), which are not potent opiate antagonists, did not reduce food intake. It is concluded that food intake is reduced by the blockade of opiate receptors. 17 references. (Author abstract modified)

003081 Saranak, Jureepan; Goldfarb, Joseph. Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, New York, NY 10029 **Effects of electrolytic and 6-hydroxydopamine lesions of the lateral hypothalamus on rotation evoked by electrical stimulation of the substantia nigra in rats.** Brain Research. 208(1):81-96. 1981.

Contralateral rotation evoked by electrical stimulation of the left substantia nigra was studied in rats before and after electrolytic or 6-hydroxydopamine (6-OHDA) lesions of the lateral hypothalamus. Electrolytic lesions, which produced mean ipsilateral striatal dopamine depletion of 58%, significantly reduced the rotation at 2 hours to 14 days postlesion. 6-OHDA lesions, which produced mean ipsilateral striatal dopamine depletion of 93%, significantly increased the rotation at 3 to 14 days postlesion. Haloperidol administration partially reduced rotation in both control and lesioned rats in a dose related manner. It is suggested that contralateral rotation evoked by electrical stimulation of the substantia nigra may reflect direct activation of neurons postsynaptic to the dopaminergic nigrostriatal neurons. 79 references. (Author abstract modified)

003082 Satinder, K. Paul. Dept. of Psychology, Lakehead University, Thunder Bay, Ontario, Canada P7B 5E1 **Interaction among d-amphetamine, scopolamine and genotype in avoidance behavior of rats.** Pharmacology Biochemistry and Behavior. 14(1):121-124, 1981.

The effects of d-amphetamine and scopolamine on avoidance behavior were determined in RHA/Lu and RLA/Lu rats. In a task in which the animal could respond in either of two directions, differences between the two lines were seen after scopolamine but not after d-amphetamine. Scopolamine was more likely than amphetamine to disrupt responsiveness to visual stimuli in the low avoidance line and this difference is influenced by bidirectional genetic selection. 8 references. (Author abstract modified)

003083 Satoh, Masamichi; Akaike, Akinori; Nakazawa, Takahiro; Takagi, Hiroshi. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan **Evidence for involvement of separate mechanisms in the production of analgesia by electrical stimulation of the nucleus reticularis paragigantocellularis and nucleus raphe magnus in the rat.** Brain Research. 194(2):525-529, 1980.

The effects of serotonergic, noradrenergic, and opiate receptor antagonists on stimulation produced analgesia (SPA) elicited from the nucleus raphe magnus (NRM) or nucleus reticularis paragigantocellularis (NRPG) were studied in male Sprague-Dawley rats. SPA elicited from the NRPG was antagonized by phenoxybenzamine (2mg/kg) and naloxone (1mg/kg), but not by methysergide (2mg/kg). SPA elicited from the NRM was inhibited by methysergide, but not by the other two drugs. Results suggest that NRM/SPA may be mediated by the serotonergic system, whereas descending noradrenergic and enkephalinergic systems may be involved in NRPG/SPA. 20 references.

003084 Savageau, Michelle M.; Beatty, William W. Beatty: Dept. of Psychology, North Dakota State University, Fargo, ND 58105 **Gonadectomy and sex differences in the behavioral responses to amphetamine and apomorphine of rats.** Pharmacology Biochemistry and Behavior. 14(1):17-21, 1981.

Apomorphine hydrochloride (2mg/kg) and d-amphetamine (5mg/kg) induced more intense and longer lasting stereotyped behavior in female rats than in male rats. Gonadectomy did not alter the drug induced stereotypy in either sex. A 1mg/kg dose of amphetamine caused greater stimulation of activity in females than in males. Castration had no effect on male drug responses, but ovariectomy blocked the stimulating effect of amphetamine on activity. Low doses of apomorphine depressed activity, and this effect was more pronounced in ovariectomized females than in the other groups. 29 references. (Author abstract modified)

003085 Scarnati, E.; Forchetti, C.; Ruggieri, S.; Agnoli, A. Dept. of Neurology, School of Medicine, University L'Aquila, I-67100 L'Aquila, Italy **Dopamine and dementia. An animal model with destruction of the mesocortical dopaminergic pathway: a preliminary study.** In: Amaducci, L., Aging of the brain and dementia, vol. 13. New York, Raven, 1980. 326 p. (p. 139-145).

An automatized psychomotor evaluation of the cerebral catecholaminergic system, in particular the dopaminergic masocortical pathway, was conducted to study the possible modification of behavioral patterns in basal conditions and during neuropharmacological treatment of Alzheimer type dementia using dopamine (DA) agonists and antagonists. The results indicate that the bilateral lesion of the DA ventral tegmental area (group A10) significantly reduced motor behavior in rats and that this impairment may be improved with the use of DA agonists and only in part by drugs releasing DA. If an ongoing study of learning confirms the presence of disturbances in avoidance behavior and if the disturbances can be corrected pharmacologically, the animal model with bilateral lesions of the A10 group will be a valid tool in studying psychomotor disturbances appearing in syndromes with involvement of the DA mesocortical system. 23 references.

003086 Schaefer, Gerald J.; Holtzman, Stephen G. Holtzman: Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Morphine-like stimulus effects in the monkey: opioids with antagonist properties.** Pharmacology Biochemistry and Behavior. 14(2):241-245, 1981.

The discriminative stimulus properties of opioids with a wide spectrum of agonist and antagonist properties were evaluated in squirrel monkeys trained to discriminate between morphine and saline in a two choice discrete trial avoidance task. Stimulus control was considered to be established when the monkeys reliably completed at least 22 trials of a 25 trial session on the lever appropriate for the drug state. Tests of stimulus generalization were conducted with compounds that were previously shown to produce discriminative stimulus effects that are morphine like, cyclazocine like, or neither morphine like nor cyclazocine like. Results confirm the heterogeneous nature of the discriminative stimulus effects of opioids with mixed agonist and antagonist properties and indicate the importance of interspecies comparisons. 17 references. (Author abstract modified)

003087 Schechter, Martin D. Dept. of Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Extended schedule transfer of ethanol discrimination.** Pharmacology Biochemistry and Behavior. 14(1):23-25, 1981.

The persistence of generalization to pentobarbital after ethanol discrimination training was studied in male Sprague-Dawley rats. Stimulus control was established with ethanol (600mg/kg) and saline in a two lever choice task and a fixed-ratio 10 schedule (Ss trained to emit a series of 10 responses on one lever) of food reinforcement. Animals were then tested with an extended schedule procedure in which lever selection and its perseverance were measured under training conditions and after pentobarbital (2 to 12mg/kg). Drug lever selection declined with decreasing doses of pentobarbital. At 4mg/kg, initial lever selection was evenly distributed between the two levers. 15 references. (Author abstract modified)

003088 Schulz, Rudiger; Wuster, Michael; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, West Germany **Differentiation of opiate receptors in the brain by the selective development of tolerance.** Pharmacology Biochemistry and Behavior. 14(1):75-79, 1981.

The development of tolerance to the delta-opiate receptor agonist D-Ala2,D-Leu5-enkephalin (DADL) or the mu-agonist sufentanyl (SUF) was studied in male Sprague-Dawley rats. In tests for catatonia, chronic intracerebroventricular infusions of DADL for 7 days produced a 15-fold tolerance with no cross-tolerance to SUF. Rats treated chronically with SUF developed tolerances to the effects of SUF on analgesia and catatonia. These animals showed no cross-tolerance to the effects of DADL on catatonia, but did show tolerance to DADL analgesia. Results suggest that prolonged stimulation of specific opiate receptors in the brain by selective agonists may bring about selective tolerance for specific receptors. These data conflict with the notion that mu-receptors specifically mediate analgesia and delta-receptors mediate catatonia. 28 references. (Author abstract modified)

003089 Scotto di Tella, A. M.; Dessaigne, S.; Mercier, J. Lab. de Pharmacodynamie, Faculte de Pharmacie, 27, bd. Jean-Moulin, F-13385 Marseille Cedex 4, France /**Can the antidepressive properties of lithium be determined experimentally?**/ Peut-on determiner experimentalement les proprietes antidepressives du lithium? Encephale. 6(2):115-129, 1980.

The antidepressant properties of lithium were studied. A sample of Swiss albino rats was divided into lots of ten each and was administered one of two types of lithium injection: a single injection of 2 or 4mEq/kg; or daily injection of the same dose over a period of 14 days. A control group was injected with sodium chloride in the same doses. The rats were administered three tests: two classic tests of antidepressants and the Porsolt test for despair; the anxiolytic effect also was studied. Results indicate that lithium did not demonstrate antiserpine, anticataleptic or central anticholinergic properties, but was able to antagonize despair behavior as measured by the Porsolt test. This effect was observed with lithium blood levels which revealed a clinically antidepressant action. 48 references. (Journal abstract modified)

003090 Seaman, Stephen Frederic. University of Pennsylvania **Dose size and interdose interval effects on morphine tolerance in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2808-B, 1981. Ann Arbor, Univ. Microfilms No. 8028888, 101p., 1980.

Factors which might affect morphine tolerance growth in the rat, dose size and interdose interval, were studied. As predicted larger doses of morphine resulted in more tolerance (less analgesia following the test doses). Likewise shorter interdose intervals resulted in more tolerance. Furthermore a multiple regression analysis suggested that the relationship between interdose interval and tolerance is linear. A number of different measures of analgesia were compared. Results indicate that the analgesic index (which corrects for both predrug latency and maximum allowable latency) yielded the most orderly results in the regression analysis, suggesting that it is a better measure of analgesia than latency, log latency, or latency area. (Journal abstract modified)

003091 Sheard, Michael H. Yale University School of Medicine, Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **Shock-induced fighting (SIF): psychopharmacological studies.** Aggressive Behavior. 7(1):41-49, 1981.

Shock induced fighting in rats is briefly reviewed and the role of catecholamine serotonin and cholinergic neuromodulation is discussed in terms of specific agonists or antagonists to each system. In studying the action on shock induced fighting, it is important to take into account: 1) differential effects on presynaptic autoreceptors and postsynaptic receptors; 2) differential effects upon forebrain versus brainstem and spinal mechanisms; and 3) the interaction between the various neuromodulating systems. These systems are a model of tightly controlled balanced regulation. This might help explain the frequent biphasic action of many drugs, as well as their frequent ineffectiveness in changing this behavior. It is also noted that the stress of the shock procedure, the stress of the fighting, and the fighting itself produce changes in the neuromodulators. These changes may synergize with or counteract the changes brought about by the drug administration itself and determine the resultant pattern which most closely correlates with the behavioral change. 41 references. (Author abstract modified)

003092 Shearman, Gary Terence. University of Rhode Island **The anxiomimetic properties of pentylenetetrazol in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):2998-B, 1981. Ann Arbor, Univ. Microfilms No. 8102536, 173p., 1980.

The hypothesis that the discriminative stimulus produced by pentylenetetrazol (PTZ) in the rat is related to its anxiogenic action in man was examined. It was also an objective to suggest the neurochemical basis for the discriminative stimulus property of PTZ through appropriate drug interactions. In an operant procedure of lever pressing, male hooded rats were trained to respond with a lever on one side of a food cup 15 minutes following a PTZ injection and to respond with a level on the alternate side following a saline injection. The anxiogenic stimulants cocaine, R05-3663, and strychnine generalized to the PTZ discriminative stimulus. The discriminative stimulus produced by PTZ was not antagonized by an anticonvulsant or other central nervous system depressants that are not anxiolytics. There was a correlation between the potency of drugs effective in antagonizing the PTZ discriminative stimulus and their effective doses in a conflict test of anxiety as well as their clinically effective doses. Generalization to the PTZ discriminative stimulus by GABA antagonists and antagonism by GABA agonists but lack of generalization to or antagonism by drugs affecting other neurotransmitter systems suggest that the PTZ discriminative stimulus might be mediated through decreased GABA neuronal activity. (Journal abstract modified)

003093 Shimizu, Takao; Koja, Takeshi; Fujisaki, Tadashi; Fukuda, Takeo. Dept. of Pharmacology, Faculty of Medicine, Kagoshima University, Kagoshima 890, Japan **Effects of methysergide and naloxone on analgesia induced by the peripheral electric stimulation in mice.** Brain Research. 208(2):463-467, 1981.

The antinociceptive effects produced by peripheral electric stimulation (PES) in mice were examined; and the influence of administration of L-5-hydroxytryptophan (5-HTP), methysergide, and naloxone on the antinociceptive effects of the PES was investigated. Administration of 5-HTP enhanced antinociceptive effects induced by PES, while methysergide and naloxone abolished this antinociception. The mechanisms of analgesia produced by PES involve both endogenous opiate systems and central serotonergic mechanisms. There is not yet sufficient evidence to determine whether the central 5-HT system or the endogenous opioid plays a more important role in producing analgesias by PES, or how the systems are interrelated. 15 references. (Author abstract modified)

003094 Sloviter, Robert S.; Damiano, Bruce P.; Connor, John D. Dept. of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, PA 17033 **Relative potency of amphetamine isomers in causing the serotonin behavioral syndrome in rats.** Biological Psychiatry. 15(5):789-796, 1980.

The relative potency of amphetamine isomers in causing the serotonin behavioral syndrome in rat was investigated. Experiments on the mechanisms by which amphetamine evokes this behavioral syndrome reveal that the l-isomer, like the d-isomer, acts indirectly, i.e., by release of endogenous serotonin. Futhermore, when d-isomer and l-isomer are compared on the basis of potency in causing the serotonin behavioral syndrome, the d-isomer is between two and three times more potent than the l-isomer. This result is consistent with the greater potency of the d-isomer (approximately two to one) in exacerbating symptoms of paranoid psychosis in humans. The data indicate that the serotonin behavioral syndrome in rats caused by relatively high doses of amphetamine may be the experimental counterpart of the paranoid psychosis induced in man by high doses of amphetamine. 24 references. (Author abstract modified)

003095 Smith, Robert C.; Biggs, Charles; Vroulis, George; Brinkman, Samuel. Section of Biological Psychiatry, Texas Research Institute of Mental Sciences, 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Effects of chronic administration of phencyclidine on stereotyped and ataxic behaviors in the rat.** Life Sciences. 28(10):1163-1174, 1981.

The effects of chronic administration of phencyclidine (PCP) on stereotyped and ataxic behaviors in the rat were investigated. After chronic administration of PCP, a high test dose (15mg/kg) of PCP produced increases in stereotypic and ataxic behaviors, and a lower test dose of PCP produced decreases in these behaviors, compared to behavioral responses of control rats. Rearing behavior in rats chronically administered PCP was increased at all test doses of the drug. Rats treated chronically with 15mg/kg PCP for 9 days showed marked increases in most of these behaviors, whereas, rats receiving 5mg/kg PCP for 9 days showed less change in several stereotypic and ataxic behaviors. Results suggest that chronic administration of PCP augments sensitivity to the sterotypic inducing effects of high doses, and decreases sensitivity to low doses of PCP. 34 references. (Author abstract modified)

003096 Spealman, Roger D.; Kelleher, Roger T.; Morse, William H.; Goldberg, Steven R. Harvard Medical School, New England Regional Primate Research Center, Southborough, MA **Supersensitivity to the behavioral effects of opiate antagonists.** Psychopharmacology Bulletin. 17(1):54-56, 1981.

Supersensitivity to the behavioral effects of opiate antagonists was examined in monkeys by determining dose effect curves for naloxone and naltrexone before and after an intervening period of chronic administration. Results from two experiments indicate that before chronic administration naloxone or naltrexone had little or no effect on responding, but after chronic administration, the cumulative dose effect curves were shifted to the left. Thus chronic administration of the specific opiate antagonists, naloxone and naltrexone, produced marked supersensitivity to their behavioral effects in squirrel and rhesus monkeys. These findings suggest that supersensitivity to the behavioral effets of opiate antagonists reflects a functional alteration of the endorphin system as a result of chronic receptor blockade. 8 references. (Author abstract modified)

003097 Steinfels, George Francis. University of Maryland Baltimore Professional Schools **Relapse to narcotic self-administration in morphine post-addict rats: a possible model for predicting abuse liability of narcotic drugs. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):2998-B, 1981. Ann Arbor, Univ. Microfilms No. 8102526, 71p., 1980.

The tendencies of rats with a previous history of narcotic addiction to relapse to narcotic drug self-administration were examined. Adult female Sprague Dawley rats were prepared with chronic EEG and EMG electrodes and intravenous cannulae. Rats were made physically dependent on morphine and then trained to lever press to receive morphine injections. After a period of withdrawal, rats who had initially received morphine, methadone, and levo-alpha-acetylmethadol (LAAM) relapsed to self-administration of morphine. A second study assessed the tendencies of morphine postaddict rats to relapse to self-administration of cyclazocine, pentazocine, nalbuphine, and butorphanol. Results suggest that there was considerable physical dependence in rats dependent on morphine and pentazocine, but relatively less physical dependence on cyclazocine, nalbuphine, and butorphanol. Data also seem to differentiate between drugs which induce both psychological and physical dependence such as morphine and pentazocine, and drugs which produce a similar psychological and apparently less physical dependence such as cyclazocine, nalbuphine, and butorphanol. (Journal abstract modified)

003098 Stevens, Robin; Goldstein, Ralph. Dept. of Psychology, Nottingham University, Nottingham, NG7 2RD England **Effects of neonatal testosterone and estrogen on open-field behaviour in rats.** Physiology & Behavior. 26(3):551-553, 1981.

The effects of neonatal testosterone and estrogen on open-field behavior in rats were investigated. On day 1 and 4 after birth, male an female rats from the same litter were injected with either testosterone propionate (TP), or estradiol benzoate (EB) or oil. Ss were tested in the open-field for 2 minutes per day, for 4 successive days at 45 and 85 days of age. Adult females were significantly more active than males in the outer and inner fields, reared more and defecated less. Neonatal TP and EB treatments reduced activity in females, but only EB increased defecation in females. EB and TP treated females were heavier than controls at 125 days of age but nonsignificantly so in the case of TP. Gonadal weights in males and females were reduced in EB and TP treatment, as were penile diameter, number of penile papillae, and anogenital spacing in EB treated males. Some of these results are consistent with the argument that androgens defeminize or masculinize certain neural mechanisms in the neonate after first being converted to estrogens, but both EB and TP have anomalous effects on males in producing morphological demasculinization. 7 references. (Author abstract modified)

003099 Takahashi, Hakuo; Bunag, Ruben D. Bunag: Dept. of Pharmacology, University of Kansas Medical Center, 39th and Rainbow Blvd., Kansas City, KS 66103 **Centrally induced cardiovascular and sympathetic nerve responses to bradykinin in rats.** Journal of Pharmacology and Experimental Therapeutics. 216(1):192-197, 1981.

Central actions of bradykinin were studied by recording blood pressure and sympathetic nerve activity from the body of a recipient rat whose head was vascularly isolated and perfused by a donor rat. Intracarotid injections of bradykinin had biphasic effects consisting of initial inhibition followed by more prolonged stimulation. Initial vasodepression and sympathetic inhibition disappeared after intracerebroventricular injection of 6-hydroxydopamine. On the other hand, the secondary pressor response and its attendant sympathetic hyperactivity were reduced after inhibition of prostaglandin synthesis with indomethacin, and conversely, augmented after administration of the prostaglandin precursor, arachidonic acid. Pressor responses elicited by intracerebroventricular injection of bradykinin in awake rats were also inhibited by indomethacin. These results indicate that bradykinin has at least two centrally induced actions on blood pressure: an initial vasodepression caused by release of endogenous norepinephrine which activates alpha-adrenergic vasodepressor mechanisms in supramedullary centers, and a secondary pressor effect that may be mediated via release of endogenous prostaglandins. 27 references. (Author abstract)

003100 Talalayenko, A. N.; Krivobok, G. K.; Boreysha, I. K. Kafedra farmakologii Donetskogo meditsinskogo instituta im. M. Gor'kogo, Donetsk, USSR /**The pharmacological analysis of monoaminergic mechanisms of the medial hypothalamus in food procuring conditioned reflexes in rats.**/ Farmakologicheskiy analiz monoaminergicheskikh mekhanizmov medial'nogo gipotalamusa v pishchedobyvatel'nykh uslovnykh refleksakh u krys. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova. 30(6):1204-1210, 1980.

Monoaminergic mechanisms of the medial hypothalamus in food procuring conditioned reflexes were studied in 16 male rats using pharmacological analysis. Results show that microinjection of noradrenaline and dopamine in the medial hypothalamus impedes the realization of the food procuring conditioned reflex, prolonging the reflex latency, lowering its value and the number of conditioned food procuring movements. The effects of catecholamines on food procuring conditioned activity are specific and are brought about through alpha-adrenoreceptors or receptors of the hypothalamic neurons sensitive to haloperidol and aminazine. Local administration of GABA to the hypothalamus prolongs the latency of the food procuring conditioned reflex, but does not change its value and the number of conditioned food procuring movements. The effect of GABA is not due to the effect on adrenoreceptors and dopamine receptors of the hypothalamus. 19 references. (Journal abstract modified)

003101 Tellez-Villagra, C.; Vazquez, F.; De la Mora, P.; Brust-Carmona, H. Brust-Carmona: Departamento de Fisiologia, Facultad de Medicina, A.P. 70250 Cd. Universitaria, Mexico 20, D. F. Mexico **Modification of motor activity, passive avoidance conditioning and evoked potentials by microinjections of strychnine in both caudate nuclei in cats.** Pharmacology Biochemistry and Behavior. 14(2):193-199, 1981.

Modification of motor activity, passive avoidance conditioning, and evoked potentials by microinjections of strychnine in both caudate nuclei in cats is described. Bilateral microinjection of 100mcg strychnine produced a stereotyped behavior of grooming and running with the extremities flexed to dark places. When placed in a two compartment chamber for passive avoidance conditioning, the cats would not move from the dark compartment to the illuminated one. After decreasing the illumination, some cats crossed to the illuminated compartment and the acquisition test was performed. Retention of the learned response was not impaired. Strychnine affected the evoked potentials recorded in caudate nucleus by nucleus centralis medialis stimulation by increasing the late positive component. In the lateral geniculate body, strychnine affected a late positive wave and in the occipital cortex it increased the initial negative peaks and decreased the late positive ones of the potentials evoked by flash stimulation. These findings suggest a more subtle role for the caudate nucleus in the regulation of visual information which is probably related to attention processes. 24 references. (Author abstract modified)

003102 Thorn, Beverly E. Southern Illinois University at Carbondale **A neuroanatomical study of analgesia and catatonia induced by etorphine in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3227-B, 1981. Ann Arbor, Univ. Microfilms No. 8102432, 79p., 1980.

The neuroanatomical substrates for etorphine hydrochloride analgesia and catatonia were investigated. Rats were injected with 1mcg etorphine in one of 11 different neuroanatomical sites: periaqueductal grey, midbrain reticular formation, cerebral aqueduct, cerebellum, basolateral amygdala, corticomedial amygdala, nucleus accumbens, caudate putamen, globus pallidus, medial thalamus or hippocampus. The Flinch jump technique was used to assess pain sensitivity and the bar test was used to study catatonia. Analgesia was never elicited without catatonia, but catatonia was elicited without analgesia, suggesting possible separation of the neuroanatomical substrate for these two opiate actions. Results show that injections of etorphine result in at least some degree of neuroanatomical specificity. (Journal abstract modified)

003103 Tompkins, E. C.; Clemento, A. J.; Taylor, Duncan P.; Perhach, J. L., Jr. Taylor: Dept. of Biologic Research, Mead Johnson Pharmaceutical Division, Evansville, IN 47721 **Inhibition of aggressive behavior in rhesus monkeys by buspirone.** Research Communications in Psychology, Psychiatry and Behavior. 5(4):337-352, 1980.

The effect of administration of buspirone or diazepam on the aggressive behavior of rhesus monkeys was investigated by measuring the response to prodding with a pole. Buspirone and diazepam exhibited antiaggressive properties in a dose dependent fashion from 20mg/kg to 160mg/kg for buspirone and at 5mg/kg and 20mk/kg for diazepam. Treatment with buspirone led to hypoactivity only at high doses, whereas all doses of diazepam which inhibited aggression elicited side-effects of both hypoactivity and ataxia. The results have implications for the use of buspirone, a new agent chemically unrelated to any existing antianxiety agent, in the treatment of psychoneurotic patients with a primary diagnosis of anxiety neurosis. 6 references. (Author abstract modified)

003104 Tulunay, F. C.; Ayhan, I. H.; Portoghese, P. S.; Takemori, A. E. Takemori: Dept. of Pharmacology, University of Minnesota, 3-260 Millard Hall, 435 Delaware St. S.E., Minneapolis, MN 55455 **Antagonism by chlornaltrexamine of some effects of delta9-tetrahydrocannabinol in rats.** European Journal of Pharmacology. 70(2):219-224, 1981.

The analgesia, hypothermia, hypothermic tolerance, and physical dependence produced by delta9-tetrahydrocannabinol (THC) in male albino rats were inhibited by chlornaltrexamine, a selective, long-acting, irreversible opiate antagonist. Results suggest that cannabis and opiates have some common features and that some actions of THC may be mediated by central opiod mechanisms. 22 references. (Author abstract modified)

003105 Valentine, Joseph O.; Barrett, James E. Dept. of Psychology, University of Maryland, College Park, MD 20742 **Effects of chlordiazepoxide and d-amphetamine on responding suppressed by conditioned punishment.** Journal of the Experimental Analysis of Behavior. 35(2):209-216, 1981.

Keypecking by two pigeons maintained under a variable-interval 2 min schedule of food presentation was suppressed when each response produced a 5 sec visual stimulus that was occasionally paired with shock. Stimulus-shock pairings occurred independently of responding according to a variable-time 6 min schedule for one bird or once per session for the other bird. The effects of chlordiazepoxide and d-amphetamine were assessed on this baseline of behavior suppressed by conditioned punishment. Chlordiazepoxide produced dose related increases in the rate of punished responding, whereas d-amphetamine produced only decreases. In addition, chlordiazepoxide produced dose related increases in response rate during the response produced and response independent stimulus presentations; d-amphetamine, however, only decreased responding during stimulus presentations. 16 references. (Author abstract)

003106 Valentino, Rita J; Herling, Seymore; Woods, James H. Dept. of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **The relationship between the acute behavioral effects of narcotic antagonists and the narcotic-dependent state.** Psychopharmacology Bulletin. 17(1):51-54, 1981.

To determine whether the behavioral effects which narcotic antagonists produce in narcotic naive and narcotic dependent animals result from common mechanisms, the discriminative stimulus properties of the prototype narcotic antagonist, naltrexone, were characterized in both morphine pretreated and normal pigeons. Naltrexone produced in each pigeon a dose related increase in responding on the naltrexone appropriate key which was maximum at 32mg/kg. Doses of naltrexone which maintained stimulus control of behavior also produced decreases in response rate. In contrast, quaternary naltrexone produced stimulus control of responding comparable to naltrexone in only one out of five pigeons, even though quaternary naltrexone was as effective as naltrexone in decreasing the rate of responding. These results suggest that the stimulus properties of naltrexone in narcotic naive animals are primarily the result of central mechanisms. 5 references. (Author abstract modified)

003107 van de Poll, N. E.; de Jonge, F.; van Oyen, H. G.; van Pelt, J.; de Bruin, J. P. C. Netherlands Institute for Brain Research, IJdijk 28 Amsterdam, The Netherlands **Failure to find sex differences in testosterone activated aggression in two strains of rats.** Hormones and Behavior. 15(1):94-105, 1981.

The effect of testosterone on intraspecific aggression in males and females of two strains of rats (WEzob and S3) was examined. Pairs of these rats, gonadectomized and treated either with oil or with testosterone propionate (TP), were tested in three different combinations: OIL, OIL against TP, and TP against TP treated animals. The results of the S3 strain indicate that testosterone treatment of either the subject or the opponents stimulates aggression in both males and females. No sex difference could be determined with respect to the incidence of aggression. In the WEzob strain a stimulatory effect of TP was shown in females but not in males. The absence of a clear stimulatory effect of TP in WEzob males in terms of changes in the total time spent on aggression, however, could suggest incorrectly that TP does not affect aggression in these animals. The possibility of TP having an effect on these males in terms of increasing the intensity of fighting is discussed. 29 references. (Author abstract modified)

003108 Venkatramaiah, S. R. S.V. University, Tirupati-517602, India **Effects of anxiety reduction by behavioural techniques and meprobamate on certain parameters of information theory.** Indian Journal of Clinical Psychology. 8(1):59-63, 1981.

The effects of anxiety reduction by behavioral programming and meprobamate on response uncertainty (RU) and information transmitted (IT) were assessed. Ss were 32 experimentally naive Wistar rats conditioned to the avoidance response by presenting a tone and a shock according to programmed procedures. Meprobamate (135mg/kg) was administered intraperitoneally. The results revealed that meprobamate decreased RU and increased IT. The findings strongly favor the hypothesis that anxiety reduction is achieved by the drug action through measurable reduction in response uncertainty. 26 references. (Author abstract modified)

003109 Villiger, John W.; Dunn, Adrian J. Dept. of Neuroscience, University of Florida College of Medicine, Gainesville, FL 32610 **Phosphodiesterase inhibitors facilitate memory for passive avoidance conditioning.** Behavioral and Neural Biology. 31(3):354-359, 1981.

Evidence is presented that a single, posttrial injection of the phosphodiesterase inhibitors Ro-20-1276 (25mg/kg and 50mg/kg) or isobutylmethylxanthine (IBMX, 75mg/kg) enhances the retention of a one trial passive-avoidance response in male ICR mice. This performance enhancement is not seen when the injection is given 1 h following task acquisition, and no footshock controls do not have lengthened step through latencies at retention testing. This suggests that these drugs facilitate memory formation. At a low dose, posttrial IBMX (25mg/kg) significantly impairs performance. These results are similar to that previously reported for papaverine and suggest that cyclic nucleotides may play a role in memory formation. 10 references. (Author abstract modified)

003110 Wagner, G. C.; Foltin, R. W.; Seiden, L. S.; Schuster, C. R. Dept. of Biopsychology, University of Chicago, Chicago, IL 60637 **Dopamine depletion by 6-hydroxydopamine prevents conditioned taste aversion induced by methylamphetamine but not lithium chloride.** Pharmacology Biochemistry and Behavior. 14(1):85-88, 1981.

The role of dopamine in conditioned taste aversion (CTA) induced by methylamphetamine in male Sprague-Dawley rats was examined. Methylamphetamine induced CTA to sweetened milk was significantly attenuated by intraventricular injection of 6-hydroxydopamine after pargyline and desmethylimipramine pretreatment. This finding indicates that the methylamphetamine induced CTA is dependent on intact dopaminergic neurons. 23 references. (Author abstract modified)

003111 Walker, J. Michael; Berntson, Gary G.; Paulucci, Thomas S.; Champney, Timothy C. Mental Health Research Institute, University of Michigan, 202 Washtenaw Pl., Ann Arbor, MI 48109 **Blockade of endogenous opiates reduces activity in the rat.** Pharmacology Biochemistry and Behavior. 14(1):113-116, 1981.

Naloxone (2mg/kg) substantially reduced general activity in 90 to 120-day-old rats under baseline conditions and after stress induced by swimming. Results suggest that endogenous opioid peptide systems may play an activational role in behavioral regulation under normal conditions as well as during stress. 27 references. (Author abstract modified)

003112 Walker, J. Michael; Berntson, Gary G.; Sandman, Curt A.; Kastin, Abba J.; Akil, Huda. Mental Health Research Institute, University of Michigan. Ann Arbor, MI 48109 **Induction of analgesia by central administration of ORG 2766, an analog of ACTH4-9.** European Jounal of Pharmacology. 69(1):71-79, 1981.

Microinjection of the ACTH4-9 analog ORG-2766 into the periaqueductal gray of male Sprague-Dawley rats produced potent, long-lasting, dose dependent analgesia. Analgesia was not observed after intracerebroventricular injections of ORG-2766. Naloxone did not reduce the analgesia induced by ORG-2766, and morhine tolerance did not diminish the effect significantly. ORG-2766 (up to 10mcM) did not inhibit 3H-naloxone binding to brain opiate receptors in vitro. Results suggest that the ACTH analog does not act through opiate mechanisms and are discussed in relation to a proposed ACTH or alpha-melanocyte stimulating hormone receptor. 33 references. (Author abstract modified)

003113 Walz, Marjorie Ann. University of Mississippi **Behavioral and metabolic alterations in progeny of methadone-treated rats. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2580-B, 1981. Ann Arbor, Univ. Microfilms No. 8028237, 140p., 1980.

The impact of chronic methadone treatment on the offspring of treated rats was assessed. Wistar rats of both sexes were given daily methadone doses of 15mg/kg for 60 days prior to mating; treatment of females was continued until weaning of pups. As compared to controls, F-1 pups of treated sires and dams showed decreased body weight, decreased viability, slowed ontogeny of reflexes, reduced exploration up to 2 weeks of age followed by an increase over controls, and decreased defecation. When only the sire received methadone, only the increase in exploratory activity and the decrease in defecation were seen. F-2 offspring showed significantly elevated neonatal mortality and decreased defecation in open-field trials. No clear changes were found in the F-3 generation. A need for clinical studies is indicated to determine how completely these findings may extraplolate to humans. (Journal abstract modified)

003114 Wellman, Paul J.; McIntosh, Pamela; Guidi, Eric. Dept. of Psychology, Texas A&M University, College Station, TX 77843 **Effects of dorsolateral tegmental lesions on amphetamine- and lithium-induced taste aversions.** Physiology & Behavior. 26(2):341-344, 1981.

Lesions of the dorsolateral tegmentum (DLT) attenuated conditioned taste aversion induced by amphetamine (2.0mg/kg), but not that induced by lithium chloride (0.15M) in female Long-Evans rats. The lesioned animals were also moderately hyperphagic. Results suggest that the aversive properties of amphetamine may be mediated by the ventral noradrenergic bundle at the level of the DLT. 28 references. (Author abstract modified)

003115 Wiechman, Beth Elaine. Purdue University **Interactions of diazepam and cocaine in the morphine-treated rat. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3000-B, 1981. Ann Arbor, Univ. Microfilms No. 8102720, 326p., 1980.

The pharmacological basis for any interaction of either diazepam or cocaine in rats representing three models of morphine treatment (morphine dependence, morphine withdrawal, and acute morphine) was investigated. Body temperature of both morphine withdrawn and acute morphine rats was less than sham implanted rats following diazepam administration. In morphine withdrawn rats, the enhanced hypothermia is likely the result of an additive effect between diazepam and morphine withdrawal, while acute morphine treatment potentiated the diazepam induced hypothermia. Doses of diazepam reduced motor coordination of all rats for at least 15 minutes. Morphine treatments altered cocaine induced changes in body temperature. Measurement of cocaine induced spontaneous locomotor activity indicated that acute morphine rats manifested depressed activity as compared with the other three groups of rats. Comparison of open-field locomotor activities induced by two other local anesthetics, procaine and lidocaine, indicated that cocaine induced stimulation of activity in morphine treated rats is unique and not shared by other local anesthetics. Although no differences in regional calcium levels were found following treatment with diazepam or cocaine, it is suggested that these drugs may alter calcium levels in one subcellular fraction, and examination of whole brain regions may mask such an effect. (Journal abstract modified)

003116 Winter, J. C. 127 Farber Hall, State University of New York, Buffalo, NY 14214 **Drug-induced stimulus control and the concept of breaking point: LSD and quipazine.** Psychopharmacology. 72(2):217-218, 1981.

Discriminative stimulus control was estabished in rats (N = 12) with lysergic acid diethylamide (LSD) and saline using a two lever response choice task and a FR10 schedule of water reinforcement. Ss were then tested once per week with either LSD or quipazine and every other week the test ratio was doubled, i.e., each drug was tested at ratios of 10, 20, 40, and 80. In contrast with LSD, which maintained stimulus control at all ratios, LSD appropriate responding following quipazine declined significantly at FR80. In addition, five of eight Ss tested with quipazine failed to complete the FR80 in 15 min. In subsequent experiments, the breaking point, which is defined as the number of LSD appropriate responses prior to emission of 10 responses on the saline appropriate lever, was determined for LSD and for quipazine. Mean values for LSD and quipazine were 161 and 65, respectively. Results suggest that conclusions regarding the stimulus properties of LSD and quipazine may be altered as a function of cross-test conditions. 7 references. (Author abstract modified)

003117 Wolf, William A.; Kuhn, Donald M.; Lovenberg, Walter. Kuhn: Section on Biochemical Pharmacology, Hypertension Endocrine Branch, NHLBI, NIH, Bethesda, MD 20205 **Pressor effects of dorsal raphe stimulation and intrahypothalamic application of serotonin in the spontaneously hypertensive rat.** Brain Research. 208(1):192-197, 1981.

The pressor effects of dorsal raphe stimulation and intrahypothalamic application of serotonin were investigated in the spontaneously hypertensive rat. Electrical stimulation of the dorsal raphe nucleus or direct microinjection of serotonin into the preoptic region of the anterior hypothalamus produces a transient rise in arterial blood pressure in both spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) controls. SHRs are more responsive to raphe stimulation but they are somewhat less responsive to serotonin injections when compared to WKYs. The serotonin antagonist metergoline blocks the pressor response to serotonin in both strains. These results suggest that the central serotonergic neuronal system plays a similar, but not identical, role in blood pressure modulation in hypertensive and normotensive rats. 25 references. (Author abstract modified)

003118 Wu, Ming-Fung; Lind, Marcia D.; Stapleton, June M.; Reid, Larry D. Rensselaer Polytechnic Institute, Troy, NY 12181 **Dose-response relationship between naloxone injections and intake of sucrose solution.** Bulletin of the Psychonomic Society. 17(2):101-103, 1981.

The effects of various doses of naloxone on the intake of sucrose solutions were investigated in rats. When individually housed rats are given, daily, a 1 hour opportunity to drink a 10% solution of sucrose, they avidly take large amounts. When given naloxone, the prototypic antagonist of morphine like effects, the intake of sucrose is attenuated. Doses as small as .065mg/kg reliably, but slightly, reduce intake and doses greater than 1.0mg/kg dramatically reduce intake. Results are discussed in relation to endorphinergic systems regulating energy balance. 10 references. (Author abstract modified)

003119 Yutrzenka, G. J.; Davis, J. S.; Parmar, S. S. Parmar: Dept. of Physiology, University of North Dakota School of Medicine, Grand Forks, ND 58202 **A possible role for catecholamine neurotransmitters in the anticonvulsant activity of chlordiazepoxide.** Research Communications in Psychology, Psychiatry and Behavior. 5(4):407-418, 1980.

The role of catecholamines in the CNS as mediators of the anticonvulsant activity of chlordiazepoxide was investigated. Chlordiazepoxide in doses of 2.5mg/kg and 5.0mg/kg provided dose dependent protection from pentylenetetrazol induced seizures in male albino mice. Treatment with either alpha-methyl-p-tyrosine, phenoxybenzamine, propranolol, or L-dopa prior to the administration of chlordiazepoxide potentiated the anticonvulsant activity of chlordiazepoxide. This was reflected by an increase in the degree of protection from convulsions, a decrease in ED50 value, and an increased time to onset of seizures in pretreated mice. Administration of disulfiram prior to the administration of chlordiazepoxide was shown to provide no significant increase in the anticonvulsant activity of chlordiazepoxide. These results indicate the role of catecholamine neurotransmitters as possible mediators of the anticonvulsant activity of chlordiazepoxide. 38 references. (Author abstract modified)

003120 Zigmond, Michael J.; Stricker, Edward M. Dept. of Biological Sciences and Psychology, University of Pittsburgh, Pittsburgh, PA 15213 **Behavioral test for detection of subclinical brain damage: an experimental model.** In: Merikangas, J., Brain-behavior relationships. Lexington, MA, Lexington Books, 1981. 217 p. (p. 93-112).

Some of the basic characteristics of catecholaminergic neurons in the brain are reviewed, evidence for compensatory neurochemical changes which appear to minimize the functional impairments produced by 6-hydroxydopamine (6-HDA) is presented, and the implications of these adaptive responses for the development of clinical instruments to detect such neuronal damage are discussed. The data show that extensive destruction of central catecholaminergic neurons has little observable impact on behavior. Following such lesions several neurochemical changes occur in residual terminals and target cells. These changes are predictable from pharmacological studies of synaptic homeostasis in intact brain and may serve to obscure the extensive neural damage. From these neurochemical effects, pharmacological challenges have been derived as diagnostic tools for detecting the presence of damage to these neuronal systems. A second approach for detecting damage has been to expose the animal to conditions which are outside the limits of compensation, thereby eliciting measurable neurological dysfunctions. 43 references.

05 TOXICOLOGY AND SIDE EFFECTS

003121 Adams, Perrie M.; Fabricant, Jill D.; Legator, Marvin S. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX 77550 **Cyclophosphamide-induced spermatogenic effects detected in the F1 generation by behavioral testing.** Science. 211(4477):80-82, 1981.

The effects of cyclophosphamide treatment of male rats and some of their female mates on the behavior of offspring were studied. Fisher 344 male rats were treated with 10 milligrams per kilogram of body weight by cyclophosphamide for 5 weeks and subsequently mated to females previously treated with saline or cyclophosphamide. Compared to controls, the first generation progeny of the cyclophosphamide treated males exhibited behavior deficits on motor reflex tests, motor coordination, and locomotor activity. It is suggested that the data could indicate a chemically induced genetic effect manifested by behavioral alterations. 12 references. (Author abstract modified)

003122 Antelman, Seymour M.; Kocan, Donna; Rowland, Neil; De Giovanni, Lesley; Chiodo, Louis A. 442 Crawford Hall, University of Pittsburgh, Pittsburgh, PA **Amitriptyline provides long-lasting immunization against sudden cardiac death from cocaine.** European Journal of Pharmacology. 69(1):119-120, 1981.

A single injection of amitriptyline conferred complete and long lasting protection against sudden cardiac death (SCD) induced by cocaine in male Sprague-Dawley rats. More than half of the rats injected with 35mg.kg i/p. cocaine died within 15 seconds. Treatment with amitriptyline (10mg/kg) 1 hour before cocaine afforded no protection against SCD. However, none of the nine rats treated with the tricyclic antidepressant 10 days prior to cocaine died, and only one of six animals treated with amitriptyline 24 hours prior to cocaine died. This protection against SCD may be related to the time dependent intensification of the effect of tricyclic antidepressants on the sensitivity of dopamine autoreceptors in the substantia nigra. 5 references.

003123 Clarke, Claire; Hobbiger, F.; Sheldon, P. W. Radiobiology Unit, Dept. of Physics, Institute of Cancer Research, Sutton, Surrey SM2 5PX, England **Acetylcholinesterase and cholinesterase activities in the mouse cerebellum following misonidazole treatment.** European Joural of Pharmacology. 69(2):209-211, 1981.

Misonidazole (five doses of 0.5mg/g i/p. over 4 days) did not alter acetylcholinesterase and cholinesterase activities in C57BL/Cbi mouse cerebellum. Enzyme inhibition occurred only with serum levels in excess of those used clinically. It is concluded that the clinical neurotoxicity of the drug cannot be attributed to an effect on cholinesterases. 6 references. (Author abstract modified)

003124 De Luca, B.; Carleo, R.; Cerciello, A.; Cioffi, L. A. Institute of Human Physiology, University of Naples, 1st Medical School, I-80138 Napoli, Italy **Cortical control of neurally mediated arrhythmogenic properties of desacetyllanatoside C.** Neuropharmacology. 20(3):297-299, 1981.

The effects of bilateral cortical spreading depression on the neurally mediated arrhythmogenic properties of digitalis were studied in Sprague-Dawley rats anesthetized with nembutal. Functional decortication significantly increased the dose of desacetyllanatoside-C required to induced cardiac effects, but did not change the basal heartrate or electrocardiogram. The higher resistance of decorticated rats may be a direct consequence of cortical ablation, but it is more likely that subcortical structures such as the hypothalamus are deprived of the excitatory influence of the cerebral cortex. 10 references. (Author abstract modified)

003125 Ford, Karen Elizabeth. University of Mississippi **Chronic effects of neuroleptics having high or low incidence of extrapyramidal side-effects upon force, duration and rate of operant response in rats. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2818-B, 1981. Ann Arbor, Univ. Microfilms No. 8028225, 207p., 1980.

A relatively new, highly effective antipsychotic compound, clozapine (CLOZ), reported to have few if any extrapyramidal side-effects (EPS) was compared with haloperidol and chlòridazepoxide in an attempt to develop animal test procedures capable of selecting other drugs with high antipsychotic activity and low EPS. Effects of drugs were compared on force, duration, and rate of response for rats performing under a FR 30 schedule of water reinforcement. The initial effects of haloperidol and CLOZ were similar in that both substantially descreased response rate and tended to increase response duration; neither drug had a large effect on peak force. Behavioral supersensitivity following termination of chronic neuroleptic treatment was not demonstrated and this failing is discussed. The ability to discriminate among haloperiodol, CLOZ, and chloridazepoxide on the basis of the discriminant function for the three dependent variables was not found to exceed greatly the discrimination provided on the basis of the linear function for the rate measure alone. Nevertheless, it is suggested that continued use of the present methodology (i.e., the combination of the joint use of intensive and rate measures of operant response and multivariate analysis methods) in future research may enable the development of a relatively economical animal model for testing new compounds with high antipsychotic efficacy but low EPS liability. (Journal abstract modified)

003126 Frigeni, V.; Bruno, F.; Carenzi, A.; Racagni, G. Zambon Farmaceutici Research Lab., Bresso, Milano, Italy **Difference in the development of tolerance to morphine and d-ala2-methionine-enkephalin in C57 BL/6J and DBA/2J mice.** Life Sciences. 28(7):729-736, 1981.

The analgesic effect elicited by intracerebroventricular (icv) administration of either morphine or d-ala2-methionine-enkephalin (d-ala2-met-enk) was studied during the onset and offset of morphine tolerance in DBA/2J (DBA) and C57 BL/6J (C57) strains of mice. DBA mice become tolerant to the analgesic effect of icv morphine after receiving eight subcutaneous (sc) injections of the ED50 of morphine for analgesia. In C57 mice tolerance to icv morphine is evident after only a single sc injection of morphine ED50. However, development of cross-tolerance to the analgesic effect of d-ala2-met-enk is similar in both strains of mice. Recovery of the analgesic effect of morphine and d-ala2-met-enk is slower in C57 than in DBA mice. 16 references. (Author abstract modified)

003127 Guinn, Meredith M.; Bedford, John A.; Wilson, Marvin C. Wilson: Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, University, MI 38677 **Antagonism of intravenous cocaine lethality in nonhuman primates.** Clinical Toxicology. 16(4):499-508, 1980.

The use of propranolol, diazepam, and chlorpromazine in the treatment of cocaine toxicity was studied in male cynomolgus monkeys. Continuous i.v. infusion of cocaine at the rate of 0.5mg/kg/minute produced a response profile in monkeys similar to the reaction" observed in humans. Chlorpromazine and diazepam both increased the seizure threshold in cocaine treated monkeys. Diazepam was more effective in protecting against convulsions, but chlorpromazine was more effective in abolishing the behavioral excitation associated with cocaine toxicity. Propranolol reduced the cardiostimulatory effects of cocaine, but enhanced some of its behavioral effects, as well as its lethality. 3 references.

003128 Laties, Victor G.; Evans, Hugh L. Dept. of Radiation Biology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Research strategies for assessing the effects of methylmercury on behavior.** Revista Mexicana de Analisis de la Conducta. 6(1):27-37, 1980.

A strategy for dealing with the assessment of the toxic effects of methylmercury on behavior is presented, based on experiments with pigeons engaged in schedule controlled behavior. The strategy consists of producing in other ways some of the signs that characterize methylmercury poisoning and of contrasting the behavioral effects of these procedures with those of methylmercury. The data obtained from several experiments show that methylmercury affects the performance of the pigeon on a schedule of reinforcement that requires discrimination of amount of behavior. This effect appears rapidly following considerable exposure to low doses of the substance. 18 references. (Journal abstract modified)

003129 Ohmoto, Takashi; Matsumoto, Yuzo; Nakamura, Shigeo; Miyamoto, Toshihiko. Dept. of Neurological Surgery, Okayama University Medical School, Okayama, Japan **Experimental studies on L-dopa induced dyskinesia.** Brain and Nerve. 32(2):161-169, 1980.

Dyskinesia induced by L-dopa was studied. Radiofrequency lesions were produced in the unilateral ventromedial tegmental area (VMT) of African green monkeys (Cercopithecus sobaeus) and tremor developed subsequently. Intraperitoneal injections of L-dopa, L-dopa combined with MK-486, ET-495, and CB-154 all relieved the tremor and induced dyskinesia. Further investigation of various centrally acting drugs and enzyme inhibitors of catecholamine metabolism in these monkeys gave evidence that dyskinesia induced by L-dopa might be due to the direct stimulation of dopamine receptors (by excessive accumulation of dopamine in the striatum). Another radiofrequency lesion, in the ventrolateral nucleus of the thalamus ipsilateral to the VMT lesion, caused the tremor to disappear and no dyskinesia was induced by the administration of L-dopa. Results suggest that: denervation supersensitivity at the postsynaptic receptors is a basic condition for L-dopa to induce dyskinesia; and the caudate nucleus is not pharmacologically uniform. 37 references. (Journal abstract modified)

003130 Pazo, Jorge H.; Tumilasci, Omar R.; Medina, Jorge H. Universidad de Buenos Aires, 2da Catedra de Fisiologia Humana, Laboratoria de Neurofisiologia, Paraguay 2155, 1121 Buenos Aires, Argentina **Studies on the mechanisms of L-dopa-**

induced salivary secretion. European Journal of Pharmacology. 69(3):255-261, 1981.

Systemic administration of L-dopa and dopamine in Wistar rats elicited a sustained secretory response in the submaxillary glands, which could be blocked by pretreatment with phentolamine plus propranolol. Acute unilateral sympathectomy (decentralization or denervation) reduced the response to L-dopa by 41 to 48%, but did not alter the response to dopamine. Chemical sympathectomy by hexamethonium caused a 45% reduction in the secretory response to L-dopa, but parasympathectomy did not modify the response to L-dopa or dopamine. Pretreatment with haloperidol reduced the salivary secretion response to L-dopa in animals with innervated glands, but not in those with denervated glands; haloperidol did not alter the response to dopamine. Results suggest that the salivary secretion induced by L-dopa is mediated by central dopaminergic receptors and peripheral adrenergic receptors. 27 references. (Author abstract modified)

003131 Rebec, George V.; Alloway, Kevin D.; Bashore, Theodore R. Dept. of Psychology, Indiana University, Bloomington, IN 47405 **Differential actions of classical and atypical antipsychotic drugs on spontaneous neuronal activity in the amygdaloid complex.** Pharmacology Biochemistry and Behavior. 14(1):49-56, 1981.

Clozapine (20.0mg/kg i.p.) typically produced a prolonged increase in activity in amygdaloid neurons in male Sprague-Dawley rats, but haloperidol (2.0mg/kg i.p.) generally failed to alter amygdaloid neuronal firing rates. The depression of firing rate induced by 1.0mg/kg d-amphetamine was reversed by clozapine, but not by haloperidol. Results suggest that neurons in the amygdaloid complex are more responsive to antipsychotic drugs devoid of extrapyramidal side-effects than to antipsychotic drugs that elicit parkinsonian like motor dysfunctions. 52 references. (Author abstract modified)

003132 Reynolds, Norman C., Jr.; Miska, Robert M. Dept. of Medicine, University of Wisconsin Medical School, 950 North 12 St., Milwaukee, WI 53233 **Safety of anticonvulsants in hepatic porphyrias.** Neurology. 31(4):480-484, 1981.

To evaluate the safety of newer anticonvulsants in hepatic porphyrias, clonazepam, carbamazepine, valproate, bromide, and paraldehyde were incubated in chick embryo hepatocyte cultures. Porphyrin was increased by carbamazepine, clonazepam, and valproate. Therefore, these agents should be avoided or used with caution in porphyric patients. It is noted that the list of unsafe agents also includes barbiturates, primidone, phenytoin, mephenytoin, ethotoin, ethosuximide, methsuximide, phensuximide, and trimethadone. Alternative approaches to acute porphyric attacks with seizures are discussed. 33 reference. (Author abstract modified)

06 METHODS DEVELOPMENT

003133 Adamec, Robert E.; King, Gary A. Scott Laboratory, Wellesley Hospital, 160 Wellesley Street East, Toronto, Ontario M4Y 1J3, Canada **Power spectral analysis of the flash-evoked after-discharge.** Electroencephalography and Clinical Neurophysiology. 51(2):201-204, 1981.

A quantitative measure of the flash evoked afterdischarge (FEAD) in the rat was derived using power spectral analysis. The utility of this method of measurement was demonstrated by quantifying the suppression of FEAD by the drug yohimbine. This method of quantification would facilitate the use of FEAD for the purpose of screening antiepileptic drugs. Spectral analysis would seem preferable to visual inspection of FEAD in terms of efficiency and reliability of measurement. It would also be preferable to simple averaging of FEADs in view of the variations in phase relationships from one FEAD to another. 4 references. (Author abstract modified)

003134 Albert, D. J. Psychology Dept., University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Infusions into the oculomotor nucleus or nerve: a method of estimating the dosage at which transmitter antagonists infused intracranially produce non-specific blocking of neural activity.** Pharmacology Biochemistry and Behavior. 14(1):67-73, 1981.

A method for estimating the dose at which nonspecific suppression effects of intracranially infused transmitter agonists appear is described. Changes in pupillary dilation are recorded after infusion of the test agent into the oculomotor nucleus or efferent oculomotor nerve. A suppression of activity in this nucleus or nerve results in pupillary dilation, whereas enhanced neural activity results in pupillary constriction. 35 references.

003135 Bernasconi, R.; Bittiger, H.; Heid, J.; Martin, P. Research Dept. of the Pharmaceuticals Division, CIBA-Geigy Ltd., Basel, Switzerland **Determination of GABA levels by a (3H)muscimol radioreceptor assay.** Journal of Neurochemistry. 34(3):614-618, 1980.

A (3H)muscimol radioreceptor assay was used to measure regional levels of GABA in male MAOI mouse brain. The method is based on the competitive inhibition of (3H)muscimol binding to the GABA receptor by GABA extracted from the tissue. The sensitivity of the assay was 5pmol GABA. The validity of the assay was confirmed by parallel gas chromatographic measurements. The technique can be used for unpurified tissue extracts. 19 references. (Author abstract modified)

003136 Bloom, F. E.; Siggins, G. R.; Henriksen, S. J. Arthur V. Davis Center for Behavioral Neurobiology, Salk Institute, San Diego, CA 92138 **Electrophysiologic assessment of receptor changes following chronic drug treatment.** Federation Proceedings. 40(2):166-172, 1981.

Considerations in the electrophysiologic assessment of receptor changes following chronic drug treatment are discussed. Electrophysiological techniques offer a direct cellular approach to questions of neurotransmitter receptor/drug interaction and are capable of providing detailed information on the functional status of receptors not readily attained from studies on disrupted cell systems. The development of improved methods for the quantitative comparison of changes in transmitter responsiveness after chronic experimental manipulations now makes possible the application of these electrophysiologic approaches to neuropharmacology. The technical and biologic considerations that underlie the analysis of these problems by electrophysiology are reviewed. In addition, some of the interpretative pitfalls are illustrated; and strategies for assessment of transmitter response are outlined. 49 references. (Author abstract modified)

003137 Calverley, Diane G.; Baker, Glen B.; Coutts, Ronald T.; Dewhurst, William G. Baker: Dept. of Psychiatry, Clinical Sciences Building, University of Alberta, Edmonton, Alberta, Canada T6G 2G3 **A method for measurement of tranylcypromine in rat brain regions using gas chromatography with electron capture detection.** Biochemical Pharmacology. 30(8):861-867, 1981.

A gas chromatography method, using electron capture detection for measurement of the monoamine oxidase inhibitor tranylcypromine (TCP) in rat brain regions, is described. The analytical method involves extraction of the drug from tissue homogenate with a liquid ion exchange resin and back extraction into acid. TCP is then acetylated and derivatized with pentafluoropropionic anhydride or trifluoroacetic anhydride for gas chromatographic analysis. Conditions for analysis on both packed and capillary columns are described. The method has been used to quantify TCP in rat brain regions after three different dosage/time schedules of TCP administration. The presence of N-acetyl-TCP has been demonstrated in brain tissue from rats treated with TCP. 21 references. (Author abstract)

003138 Horsburgh, Ross J. Dept. of Psychiatry, School of Medicine, University of Auckland, Private Bag, Auckland, New Zealand **Increases in skin resistance of white rats following scopolamine injection.** Pharmacology Biochemistry and Behavior. 14(1):1-3, 1981.

Male Sprague-Dawley rats were injected with saline or 0.6mg/kg scopolamine and placed on a metal grid. The grid was wired to a transistor based detector that determined whether the animal's resistance was above or below a preset threshold value. Over 5 minute test sessions, rats treated with scopolamine had resistances above each of the three threshold values used (5, 10, and 15 megohms) for significantly longer than did control rats. Since increases in resistance usually lower the shock received, this drug induced alteration in resistance should be taken into account in certain pharmacological experiments. 12 references. (Author abstract modified)

003139 Lackovic, Z.; Parenti, M.; Neff, N. H. Neff: Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Simultaneous determination of femtomole quantities of 5-hydroxytryptophan, serotonin and 5-hydroxyindoleacetic acid in brain using HPLC with electrochemical detection.** European Journal of Pharmacology. 69(3):347-352, 1981.

A method for the determination of 5-hydroxytryptophan, 5-hydroxytryptamine, and 5-hydroxyindoleacetic acid in brain is described. Brain proteins are precipitated with Zn(OH)2. The indoles in the supernatant are separated by high pressure liquid chromatography in less than 8 minutes on a reverse phase column and detected electrochemically. As little as 38fmole of hydroxyindole compound can be detected and quantitated. 15 references. (Author abstract modified)

003140 McKinney, William T., Jr. University of Wisconsin Medical School, Madison, WI 53706 **/Pharmacological evidence for catecholamine involvement in animal aggression./** Discussion of paper by Dr. Klaus Miczek. Psychopharmacology Bulletin. 17(1):62-63, 1981.

Methodological issues in the study of catecholaminergic involvement in animal aggression are discussed. It is contended that there is a great need to dissect behavioral effects into their components and to describe the total social effects of a drug. In an ethological sense, this involves careful understanding of the precipitants, description of the behaviors into their component parts, sequential aspects, and consequences. It is noted that aggressive behaviors are often species specific, and are sometimes misinterpreted. (Author abstract modified)

003141 Mori, Junko; Hori, Nobuaki; Katsuda, Nobuo. Dept. of Physiology, National Defense Medical College, Tokorozawa, Saitama 359, Japan **A new method for application of horseradish peroxidase into a restricted area of the brain.** Brain Research Bulletin. 6(1):19-22, 1981.

A new method for application of horseradish peroxidase (HRP) into very restricted brain areas is described. Crystalline HRP was packed into the tips of fine micropipettes having tip size of about 50 mcm in outer diameter. The HRP micropipettes were stereotaxically implanted into the globus pallidus of rats. After survival period of 6 to 48 hours, brain was excised and HRP distribution was investigated following conventional procedures. The diffusion area of HRP at the application sites was restricted within the limits of 200 to 250 mcm in diameter completely inside the globus pallidus. It is shown that the slowly solubilized crystalline HRP was taken up by the nerve terminals in the globus pallidus, and transported retrogradely to the cell bodies in the pars compacta of substantia nigra, indicating the existence of nigro/pallidal projections. 20 references. (Author abstract modified)

003142 Ostrow, David G.; Southam, Arthur S.; Davis, John M. Psychiatary Section, Lakeside V.A. Hospital, Northwestern University Medical School, 333 East Huron St., Chicago, IL 60611 **Lithium-drug interactions altering the intracellular lithium level: an in vitro study.** Biological Psychiatry. 15(5):723-739, 1980.

An in vitro incubation system using a bicarbonate/CO2 buffer system which can predict accurately the in vivo red cell:plasma lithium ratio (LR) is described. Piperazine phenothiazines produced the most marked elevations of intracellular lithium, doubling the LR when added to the system. The aminoalkyl phenothiazines and thioxanthenes were somewhat less active, while the nonphenothiazine antipsychotics, such as loxapine, haloperidol and molindone, produced only minor increases in the LR. Tricyclic antidepressants produced a 20% to 30% increase, while other types of antidepressants, the major neurotransmitters and their metabolites, hormones, benzodiazepines and diuretics did not show any activity. of the antihypertensives studied, only hydralazine had an effect on the LR. The effect of fluphenazine on the intracellular lithium level was paralleled by an increase in intracellular sodium and was blocked by dipyridamole. Several important lithium/drug interactions may contribute to an increased LR. Caution is urged in interpretation of studies of the relationship between the LR and clinical aspects of the affective disorders. 52 references. (Author abstract modified)

003143 Palermo, Nick N.; Brown, H. Keith; Smith, Donn L. Brown: Dept. of Pharmacology and Therapeutics, University of South Florida, College of Medicine, 12901 North 39th St., Tampa FL 33612 **Selective neurotoxic action of capsaicin on glomerular C-type terminals in rat substantia gelatinosa.** Brain Research. 208(2):506-510, 1981.

The selective neurotoxic action of capsaicin on glomerular C-type terminals in rat substantia gelatinosa was demonstrated. Since the C-terminals may be essential components of the circuitry for modulation of pain, it is suggested that capsaicin induced analgesia is the result of this neurotoxic action. It is speculated that capsaicin may prove to be a useful tool in determining the role of glomerular C-type terminals in this and other sensory relay nuclei. Data indicate that the selective neurotoxic action of capsaicin for glomerular C-type terminals is linked to substance-P depletion in the substantia gelatinosa. 18 references. (Author abstract modified)

003144 Purves, Robert. Dept. of Anatomy and Embryology, University College London, Gower Street, London WC1E 6BT, England **Ionophoresis -- progress and pitfalls.** Trends in NeuroSciences. 3(10):245-247, 1980.

The neurobiological technique of ionophoresis (iontophoresis), the release of substances from micropipettes by electric currents, is reviewed. It is noted that the method was invented by Nastuk, who used an electrically controlled microjet of acetylcholine to mimic the physiological behavior of the nerve terminal during neuromuscular transmission. Del Castillo and Katz exploited the localized nature of ionophoretic release to map the distribution of acetylcholine receptors on the membrane of muscle fibers. Currently, the chief uses of ionophoresis include: microapplication of drugs or neurotransmitters to the surface of suitably receptive cells; intracellular injection of fluorescent dyes or other markers; intracellular injection of drugs; and alteration of intracellular ion concentrations. 14 references. (Author abstract modified)

003145 Slaughter, Malcolm M.; Miller, Robert F. Dept. of Opthalmology, Washington University School of Medicine, St. Louis, MO 63110 **2-Amino-4-phosphonobutyric acid: a new pharmacological tool for retina research.** Science. 211(4478):182-185, 1981.

The use of 2-amino-4-phosphonobutyric acid as a new pharmacological tool for retina research is described. It is noted that information processing in the vertebrate retina occurs in two separate channels known as on and off channels. When intracellular electrophysiological recordings were obtained from the perfused retina eyecup preparation of the mudpuppy (Necturus maculosus), the addition of 2-amino-2-phosphonobutyric acid to the bathing medium blocked all responses in the on channel but left intact the off responses including off ganglion cell discharge. 2-Amino-4-phosphonobutyric acid blocks the light response of the on bipolar cell by mimicking the endogenous photoreceptor transmitter. 13 references. (Author abstract modified)

003146 Towell, John F.; Erwin, V. Gene. School of Pharmacy, University of Colorado, Boulder, CO 80309 **Characterization of the isolated perfused mouse brain as a system for neurochemical studies.** Brain Research. 209(2):476-481, 1981.

The preparation of the isolated perfused mouse brain (IPMB) is described along with its electrophysiological, morphological, biochemical, and pharmacological properties. Using high performance liquid chromatography with electrochemical detection, the primary metabolite of mammalian CNS norepinephrine, 3-methyoxy-4-hydroxyphenethyleneglycol (MHPG) was measured in the perfusate at 15 minute intervals. The rate of MHPG production was found similar to literature values of the rate of norepinephrine turnover in mouse brain. MHPG production rate in the IPMB was blocked by pretreatment with 6-hydroxydopamine and was increased by pretreatment with reserpine. 22 references. (Author abstract)

003147 Wieraszko, Andrzej. Dept. of Biochemistry of the Nervous System and Muscle, Nencki Institute of Experimental Biology, Pasteura 3, 02-093 Warszawa, Poland **Modified cup technique for microestimation of the release and uptake of neurotransmitters in brain slices.** Brain Research. 194(2):561-565, 1980.

A modified cup technique for determining the intensity and localization of the uptake and release of neurotransmitters in brain slices is described. The technique can be used to map uptake and release processes in various regions of the slice following electrical or chemical stimulation. The use of this technique to study glutamate uptake and release in hippocampal slices is described. 15 references.

003148 Yoshino, Jun E.; Baxter, Daniel E.; Hsiao, Ting H.; McClure, William O. McClure: Section of Cellular Biology, Dept. of Biological Sciences, University of Southern California, Los Angeles, CA 90007 **Release of acetylcholine from rat brain synaptosomes stimulated with leptinotarsin, a new neurotoxin.** Journal of Neurochemistry. 34(3):635-642, 1980.

The effect of leptinotarsin, a neurotoxin protein found in the hemolymph of potato beetles of the genus Leptinotarsa, was studied in male Sprague-Dawley rat synaptosomes preloaded with (3H)choline. Leptinotarsin from two species, L. haldemani (leptinotarsin-h) and L. decemlineata (leptinotarsin-d), induced the release of radioactivity. However, the kinetics and dose/release curves of toxins from the two species differed. Toxins from both species were partially purified, and leptinotarsin-h did not appear to be identical to leptinotarsin-d. The purified toxins prove to be useful tools for studying the release of acetylcholine. 15 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

003149 Boucharlat, Jacques. Centre de Psychotherapie, C.H.U., Hopital Sud de Grenoble, F-38130 Echirolles, France /**Perspectives on Prazinil (carpipramine): a disinhibiting agent with no neuroleptic activity. A review of 38 cases.**/ Le point sur le Prazinil ou carpipramine: un medicament desinhibiteur sans pouvoir neuroleptique. A propos de 38 observations. Psychologie Medicale. 12(13):2801-2807, 1980.

A study was conducted to verify the clinical properties of carpipramine. Previous studies have shown carpipramine to be effective in treating schizophrenics with deficiency syndrome, depressive syndromes, asthenic syndromes due to detoxification, and psychasthenic states. The majority of patients of the 38 cases, 26 were followed to conclusion were schizophrenics with apragmatism predominating. Overall results, as well as tolerance, were good. 17 references.

003150 Calandra, C.; Roxas, M.; Rapisarda, V. Universita degli Studi di Catania, Clinica Psichiatrica, Catania, Italy /**The antidepressant action of sulpho-adenosyl-L-methionine (SAMe) compared with that of chloripramine: hypothetical interpretations of the mechanism of action.**/ Azione antidepressiva della SAMe a paragone della clorimipramina: ipotesi interpretativa del meccanismo d'azione. Minerva Psichiatrica. 20(2):147-152, 1979.

The treatment of depressed patients with sulpho-adenosyl-L-methionine (SAMe), as opposed to chlorimipramine, was studied through personal experience. The sample consisted of 24 depressive patients, between ages 18 and 76, who were divided into two groups of 12 subjects each. The first group was treated with 100 mg of chlorimipramine daily for 15 days; the second group was administered 150mg of SAMe daily for the same period of time. The results indicate that both drugs have the same degree of antidepressant activity. Reference is made to the fact that the SAMe was tolerated perfectly and did not cause any unwanted side-effects. 16 references. (Journal abstract modified)

003151 Caldwell, Henry C.; Westlake, Wilfred J.; Schriver, Robert C.; Bumbier, Edgar E. Research and Development Division, Smith Kline and French Laboratories, Philadelphia, PA 19101 **Steady-state lithium blood level fluctuations in man following administration of a lithium carbonate conventional and controlled-release dosage form.** Journal of Clinical Pharmacology. 21(2):106-109, 1981.

Steady-state lithium blood level fluctuations were examined in 16 normal volunteers following administration of lithium carbonate in conventional immediate release form and in a controlled release dosage form. These cross-over studies at steady-state show that the controlled release tablet produced a smoother curve than did the conventional capsule with no loss of total bioavailability. Quantitatively, the capsule produced about 1.4 times more fluctuation in serum lithium values than did the tablet. 9 references. (Author abstract modified)

003152 Chabrand, Pierre; Pandelon, Rene. Centre Hospitalier Regional, F-30006 Nimes Cedex, France /**An open study of maprotiline 75mg in the treatment of depressive states.**/ Etude ouverte de la maprotiline 75mg dans le traitement des etats depressifs. Psychologie Medicale. 12(3):695-701, 1980.

The effect of maprotiline on 20 psychiatric patients was studied. The majority of Ss received 75mg of maprotiline in a single evening dose; the rest received 150mg in a single evening dose. The length of treatment ranged from 3 weeks to 3 months. Results show that the thymoanaleptic effect is comparable to that of the tricyclic antidepressants and that tolerance of maprotiline is better. Changes in mood occurred rapidly, within 3 to 7 days of the onset of treatment. The single dose of maprotiline is thought to represent an advantage in outpatient treatment and to facilitate an improved tolerance of the drug. 77 references. (Journal abstract modified)

003153 Conde-Lopez, Valentin. Facultad de Medicina, Valladolid, Spain /**A double-blind crossed clinical study with a new psychopharmaceutical: tiadipone (QM-6008), diazepam, and a placebo.**/ Estudio clinico doble ciego cruzado con un nuevo psicofarmaco: la tiadipona (QM-6008), diacepam y placebo. Actas Luso-Espanolas de Neurologia, Psiquiatria etc. 8(6):409-442, 1980.

The chemical characteristics of a new psychotropic drug, tiadipone, or QM-6008 (6,7-tetramethylene-5-phenyl-1,2-dihydro-3H-thieno-(2,3-e)-1,4-diazepin-2-one) and the basic pharmacological findings in humans and animals are described. Two clinical neuropharmacological steps were performed: the double-blind crossed clinical design with tiadipone, diazepam, and piridoxine base as a placebo, and the controlled parameters, including Zung's Self-Rating Depression scale of symptoms translated into Spanish, the Hamilton Depression Scale, and Overall's Brief Psychiatric Rating Scale. The results show that tiadipone does not present either clinical or psychometric antidepressive effects. No significant differences were found in the anxiolytic benzodiazepinic action of tiadipone and diazepam. There were no side-effects from psychostimulant effects. A dosage of 75mg per day in three doses was found to be the most effective. 28 references. (Journal abstract modified)

003154 DeVane, C. L.; Savett, M.; Jusko, W. J. Jusko: Clinical Pharmacokinetics Laboratory, Millard Fillmore Hospital, 3 Gates Circle, Buffalo, NY 14209 **Desipramine and 2-hydroxy-desipramine pharmacokinetics in normal volunteers.** European Journal of Clinical Pharmacology. 19(1):61-64, 1981.

Disposition characteristics of desipramine and its metabolite, 2-hydroxy-desipramine, were determined in four healthy male volunteers following an oral 50mg dose of desipramine. Nonlinear least-squares regression of concentration time data indicate that parent drug disposition could be described by a one compartment open pharmacokinetic model for two Ss and by a two compartment model for two other Ss. The early appearance of 2-hydroxy-desipramine and its peak concentration indicate that desipramine probably undergoes presystemic elimination partly through formation of 2-hydroxy-desipramine. The substantial production of 2-hydroxy-desipramine, as reflected by the area under its concentration time curve which was 51% to 94% of that for the desipramine, indicates that accumulation will occur following multiple dosing. As 2-hydroxy-desipramine may possess antidepressant activity, future studies designed to assess the therapeutic effect of desipramine should account for the presence of its pharmacologically active metabolite. 18 references. (Author abstract)

003155 Dordain, G.; Puech, A. J.; Hecquet, S.; Paturaud, J. P.; Simon, P. Clinique Neurologique, C.H.U. de Clermon-Ferranc, B.P. 69, F-63003 Clermont-Ferrand Cedex, France /**Difficulties encountered during a controlled study of a new hypnotic drug (triazolam) by a group of general practitioners.**/ Difficultes rencontrees lors de la realisation de l'essai controle d'un nouvel hypnotique (triazolam) par un groupe d'omnipraticiens. Therapie. 35(1):119-124, 1980.

The efficacy of a new hypnotic drug, triazolam, was compared to that of nitrazepam. Ten physicians were instructed to conduct an experiment involving both drugs with a total of 47 patients. Any subjects experiencing insomnia were instructed to take one medication one night and the other medication the next night. Each subject recorded the following data: time needed to fall asleep, quality and duration of sleep, number of times awakened, the quality of morning wake-up, concentration capacity during the morning, and dreams. Results indicate that 28 subjects expressed a preference for triazolam, 11 for nitrazepam, and 8 expressed no preference. The recorded data showed improvement in every area with two exceptions: dreams and morning concentration capacity were the same for both drugs. 1 reference.

003156 Duizabo, Ph. Hopital Suisse, 10, rue Minard, F-92130 Issy-les-Moulineaux, France **/A new dopaminergic agent in current psychiatric practice./** Un nouvel agent dopaminergique dans la pratique psychiatrique courante. Psychologie Medicale. 12(7):1579-1585, 1980.

The use of amineptine, a new dopaminergic agent, in everyday psychiatric practice was studied. Thirty five patients, suffering from depression, neurosis, and psychosis, were given 200mg of amineptine daily for 3 months. Each subject was examined before treatment, after 15 days, after 1 month, and after 3 months. Results indicate that 90% of the subjects responded positively to the drug. The antidepressant properties of the drug alleviated the signs of depression and improved apathetic or indifferent behavior, allowing social and occupational rehabilitation of the patients. 52 references. (Journal abstract modified)

003157 Fenelli, A.; Pierelli, F.; Koverech, A.; Calvani, M.; Le Pera, G.; Nava, D. Clinica **/Tolerance in a compressed gastroresistant form in psychiatric patients./** Tollerabilita della depamide in compresse gastroresistenti in pazienti psichiatrici. Lavoro Neuropsichiatrico. 64(1/2):67-73, 1979.

The tolerance of a new form of Depamide was studied. A sample of 20 psychiatric patients was administered 300mg of Depamide in a compressed gastroresistant form three times daily (900 to 1800mg per day). Results show that of 20 subjects, only 4 demonstrated gastric intolerance to the drug and abandoned therapy. The remaining subjects did not show any undesirable side-effects. It is concluded that this form of treatment is beneficial for patients in long-term therapy. 12 references. (Author abstract modified)

003158 Fenelli, A.; Pierelli, F.; Koverech, A.; Calvani, M.; Le Pera, G.; Nava, D. Clinica **/Tolerance study in psychiatric patients of a new preparation of sodium dipropylacetate./** Studio sulla tollerabilita in pazienti psichiatrici di una nuova preparazione a base di dipropilacetato di Na. Lavoro Neuropsichiatrico. 64(1/2):75-79, 1979.

The use of a new Form of Depakin (sodium dipropylacetate) in the treatment of psychiatric patients was studied. A sample of 33 subjects was divided into two groups. The first group consisted of 18 subjects who were treated with nongastroresistant Depakin; the second group consisted of 16 subjects who were treated with 200mg of gastroresistant Depakin. Results indicate that the group treated with gastroresistant Depakin demonstrated optimum tolerance in long-term treatment with very few side-effects, particularly in cases of organic pathology. 8 references. (Author abstract modified)

003159 Mann, Martha; Michael, Sandra D.; Svare, Bruce. Svare: Dept. of Psychology, State University of New York, 1400 Washington Ave., Albany, NY 12222 **Ergot drugs suppress plasma prolactin and lactation but not aggression in parturient mice.** Hormones and Behavior. 14(4):319-328, 1980.

The role of pituitary prolactin (PRL) in the maternal aggressive behavior of mice was investigated. It was found that daily administration of pituitary PRL inhibitors (ergocornine hydrogen maleate and 2-bromo-alpha-ergocryptine) to parturient Rockland-Swiss Albino mice suppresses circulating level of PRL and lactation, but fails to alter maternal aggession toward adult male intruders. The results suggest that, contrary to popular speculation, PRL may not be necessary for postpartum aggression in the mouse. They support the view that lactogenic hormones are not involved in mammalian maternal aggression and suggest the need for exploring the possibility that more direct manipulations of neurotransmitters systems via specific agonists and antagonists alter agrression in parturient mice. 26 references. (Author abstrct modified)

003160 no author. no address **FDA clips psychodrug pioneer's IND wings.** Medical World News. 22(4):9-10, 1981.

FDA action taken against Dr. Nathan S. Kline, controversial advocate of chemical answers to mental ills, is reported. Dr. Kline has been barred from using investigational drugs on people. Documents indicate that he used the peptide beta-endorphin before its safety ahd been demonstrated, continued to use clozapine even after being ordered to stop, and did not keep adequate documentation concerning patients he was treating and procedures he was using. Another controversy involving Dr. Kline and his acceptance of a $10,000 Lasker prize is discussed.

003161 Ochs, Hermann R.; Bodem, G.; Greenblatt, D. J. Medizinische Universitatsklinik, D-5300 Bonn-Venusberg, West Germany **Effect of dose on bioavailability of oral digoxin.** European Journal of Clinical Pharmacology. 19(1):53-55, 1981.

The effect of dosage level on bioavailability was examined in nine healthy volunteers who received single .25, .5, 1.0, 1.5, and 2mg doses of oral digoxin tablets in random sequence on five occasions separated by at least 4 weeks. Urinary excretion of immunoassayable digoxin was determined from eight consecutive 24 hr urine samples collected after each dose. Mean values of cumulative urinary excretion of digoxin at the five doses were 40.9%, 35.6%; 36.4%; 34.1%; and 33.5% of the dose (F=.64; d.f.=4.32; N.S.). Mean values of urinary excretion half-life were 2.48, 2.03, 2.20, 2.07, and 1.87 days (F=2.87; d.f.=4.32; p.=.05). Thus, bioavailability of orally administered digoxin tablets in healthy volunteers is dose dependent over an eightfold range of doses. 9 references. (Author abstract modified)

003162 Roufogalis, Basil D. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, V6T 1W5 Canada **Calmodulin: its role in synaptic transmission.** Trends in NeuroSciences. 3(10):238-241, 1980.

Research leading to the hypothesis that calmodulin can mediate many Ca2 dependent processes in synaptic transmission and plays a role in the interactions between neurotransmitters, Ca2, and cyclic AMP is reviewed, and the mechanisms by which the regulation of calmodulin may control the sequence of events during synaptic activation are examined. It is noted that there is considerable evidence that calmodulin mediates most Ca2 dependent processes and hence, may regulate presynaptic and postsynaptic events. Calmodulin can also regulate the metabolism of cyclic AMP and is itself regulated by cyclic AMP. 11 references. (Author abstract modified)

003163 Silva, Clodomir C.; Campos, Fatima; Carlini, E. A. Depto. de Fisiologia, Centro de Biociencias, Universidade Federal do Rio Grande do Norte (UFRN), Natal, Brazil **Aggressive behavior induced by apomorphine in rats submitted to four stressful situations.** Research Communications in Psychology, Psychiatry and Behavior. 5(4):353-367, 1980.

The aggression inducing property of apomorphine and bodyweight loss were studied in controls and in rats previously submitted to four stressful situations (REM sleep deprivation, cold water swimming, electrical shocks to the paws, and immobilization). Aggressiveness was observed in Ss submitted to REM sleep deprivation or to shock over 2 or 3 day periods. Shorter periods of REM sleep deprivation or foot shocks, as well as swimming or immobilization for 2 to 3 days, failed to facilitate apomorphine side-effects on aggression. There was no relationship between weight loss and the capability of apomorphine to induce aggressive behavior in the stressed rats. 18 references. (Author abstract modified)

003164 Stern, Stephen L. University of Pennsylvania, Philadelphia, PA 19104 **Rapidity of clinical antidepressant response to imipramine. (Unpublished paper).** Final Report, NIMH Grant R01-MH-31870, 1980. 13 p.

A simple test for predicting the daily dosage of imipramine (IMI) that would achieve optimal plasma concentrations of IMI plus its metabolic desipramine (DMI) at steady-state in individual depressed patients was developed and validated. A high correlation was found between 24 hour and steady-state plasma concentrations of IMI and DMI in 20 normal volunteers, who were treated with a 25mg of IMI daily. In a second experiment, nine depressed males were given 50mg of IMI orally, an optimal daily dosage was predicted for each patient to produce a combined plasma level of IMI and DMI of 250ng/ml at steady-state, and the mean combined level was found to be 326ng/ml for seven Ss. Results of this study do not indicate that this procedure was a more accurate predictor than was the 24 hour level. A table for the prediction of a patient's optimal dosage in Experiment 1, based on this correlation and on the assumption that the relationship between dosage and plasma levels in linear for a patient treated with IMI, is given. Suggestions for further research are given. 10 references.

08 DRUG TRIALS IN SCHIZOPHRENIA

003165 Bigelow, Llewellyn B.; Weinberger, Daniel R.; Wyatt, Richard Jed. William A. White Division, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Synergism of combined lithium-neuroleptic therapy: a double-blind, placebo-controlled case study.** American Journal of Psychiatry. 138(1):81-83, 1981.

A longitudinal, placebo controlled case study is described of the response to drug treatment in a 64-year-old female schizoaffective patient hospitalized for 40 years. While neither lithium nor a neuroleptic drug alone was effective, both drugs administered simultaneously led to the gradual extinction of a pronounced behavioral cycle and the disappearance of manifest psychosis. A synergistic interaction between the two drugs is suggested, and the need for sustained trials of the combination therapy in patients with similar behavioral cycles is emphasized. 11 references. (Author abstract modified)

003166 Brown, Walter Armin; Laughren, Thomas. VA Medical Center, Davis Park, Providence, RI 02908 **Low serum prolactin and early relapse following neuroleptic withdrawal.** American Journal of Psychiatry. 138(2):237-239, 1981.

Research evidence is reported from a study of 28 schizophrenic patients over 10 months to demonstrate that those with low serum prolactin concentrations during maintenance neuroleptic treatment relapse earlier than those with higher serum prolactin concentrations. Although the relative bioavailability of neuroleptic would appear a likely explanation, the data do not support this hypothesis. The findings suggest that some patients have a modest prolactin rise at the onset of treatment, show a marked dimunition with continued treatment, and tend to early relapse when neuroleptic is discontinued. Others have a more robust increase at onset, show a less dramatic drop during treatment, and remain clinically stable for a longer period of time after withdrawal. These two groups may have a different neurophysiologic substrate that underlies differences in prolactin regulation and clinical course. 10 references.

003167 Buchsbaum, M. S.; Davis, G. C.; van Kammen, D. P. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Diagnostic classification and the endorphin hypothesis of schizophrenia: individual differences and psychopharmacological strategies.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 177-194).

The endorphin hypothesis of schizophrenia is reviewed as a case history of research, as a target for psychophysiological and neuropharmacologic approaches, and as a potentially viable but limited factor in mental dysfunction. Direct evidence for the endorphin hypothesis, indirect evidence (pain sensitivity, electrophysiological measures of sensory sensitivity, and opiate antagonists and evoked potential amplitude) for a role of endorphins in schizophrenia, and specificity of pain insensitivity findings for schizophrenia are discussed, and new strategies for identifying subgroups of schizophrenic patients are considered. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. 62 references.

003168 Carman, John Scott; Bigelow, Llewellyn B.; Wyatt, Richard Jed. Dept. of Psychiatry, University Hospital, Birmingham, AL 35294 **Lithium combined with neuroleptics in chronic schizophrenic and schizoaffective patients.** Journal of Clinical Psychiatry. 42(3):124-128, 1981.

In a placebo controlled double-blind cross-over study, lithium carbonate was added to the neuroleptic treatment of 11 chronic schizophrenic and seven schizoaffective inpatients. Nurses' ratings of behavior indicate significant improvement in eight patients in agitation or manic behavior, five patients in psychosis, and five patients in depression. A greater initial severity of symptoms, presence of affective symptoms, and episodic course characterized the favorable response group. No neurotoxicity was encountered in this study. 26 references. (Author abstract)

003169 DeLisi, L. E.; Wise, C. D.; Bridge, T. P.; Rosenblatt, J. E.; Wagner, R. L.; Morihisa, J.; Karson, C.; Potkin, S. G.; Wyatt, R. J. Adult Psychiatry Branch, Division of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **A probable neuroleptic effect on platelet monoamine oxidase in chronic schizophrenic patients.** Psychiatry Research. 4(1):95-107, 1981.

Platelet monoamine oxidase activity (MAO) was studied serially over time in 16 chronic schizophrenic patients when medication free and then when medicated. Thirteen of the 16 patients had significant decreases in platelet MAO activity following neuroleptic drug treatment. The change in MAO activity was found to be correlated with response to treatment and to dose of medication. Results are discussed in terms of previous research. 56 references. (Author abstract modified)

003170 Erban, L.; Prokes, J.; Richtrova, E. Research Institute of Psychiatry, CS-131 03 Praha 8, Czechoslovakia **Plasma level**

of cyclic AMP and mental diseases. Activitas Nervosa Superior. 22(4):269-273, 1980.

Plasma cyclic AMP levels of schizophrenic Ss and normal control Ss were monitored and compared. In the first phase, 12 patients without active therapy were compared to a control group of 16 hospital employees who ate the same food as the patients. In the second phase cyclic AMP was determined in eight patients before and after 2 weeks and 4 weeks of chlorpromazine therapy. In the third phase, 14 patients still on medication were compared with 14 control Ss. It is concluded that cyclic AMP levels are a measure of the unspecific reaction of the patient's motor activity. It is noted that the elevated plasma cyclic AMP levels in schizophrenic Ss after discontinuation of neuroleptic therapy agrees with similar findings of urinary cyclic AMP in the manic phase of manic-depressive patients. 39 references.

003171 Freeman, Hugh L. Hope Hospital, Eccles Old Road, Salford M6 8HD, England **Long-term treatment of schizophrenia.** Comprehensive Psychiatry. 22(1):94-102, 1981.

Issues in the long-term treatment of schizophrenia are examined from a biopsychosocial perspective. Results of an English study of 190 chronic schizophrenics suggest that interaction between drug side-effects, environmental stimuli, and psychophysiological sensitivity may contribute to relapse in deinstitutionalized patients, despite maintenance of apparently adequate levels of medication. The role of neuroleptics in long-term treatment is then considered in terms of their influence on patterns of service delivery, their efficacy in preventing acute relapses, and their impact on the overall prognosis of schizophrenia. Considerable evidence is now available which indicates that the prognosis of schizophrenia can be considerably improved by neuroleptic maintenance therapy, particularly with the new depot drugs. However, in view of the importance influence of the family environment and the service network on long-term maintenance, medical efforts must be related to social and occupational rehabilitation, applied with skill and care in an integrated and comprehensive fashion. 20 references.

003172 Gamburg, A. L.; Aranovich, A. G.; Kotel'kevich, Yu. N.; Omorokov, B. M.; Rasnyuk, V. A.; Severinova, N. P. Kafedra psikhiatrii Saratovskogo meditsinskogo instituta, Saratov, USSR **/Treatment of therapeutically resistant paranoid schizophrenic patients with fluphenazine depot combined with other psychotropic drugs and clozapine./** Lecheniye moditenom-depo s drugimi psikhotropnymi sredstvami i leponeksom terapevticheski rezistentnykh bol'nykh paranoidnoy shizofreniyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(8):1211-1216, 1980.

The treatment of therapeutically resistant paranoid schizophrenic patients with fluphenazine depot, with other psychotropic drugs and with clozapine was instituted in 251 patients (78 women and 173 men ranging in age from 16 to 50 years). The results of treatment with these drugs were compared. Findings indicate that a comprehensive treatment may be applied successfully to some paranoid schizophrenics resistant to fluphenazine depot and other neuroleptic drugs or their combinations. Comprehensive treatment appears to be more effective in cases of systematized delusions, psychic automatism syndromes, and in crude emotional volitional defect. Treatment with clozapine is more efficacious in emotionally saturated nonsystematized delusions, pronounced disordered behavior, and mild manifestations of deterioration. 18 references. (Journal abstract modified)

003173 Giannelli, A.; Vallillo, R. Servizi Psichiatrici Provinciali, Bergamo, Italy **/Considerations on long-acting chemotherapy: an experience with fluphenazine decanoate./** Osservazioni in tema di chemio-terapia long-acting: a proposito di una esperienza con flufenazina decanoato. Rivista Sperimentale di Freniatria. 103(1):164-174, 1979.

The important aspects of long-lasting neuroleptics were analyzed in 86 schizophrenic patients (42 women and 44 men) who were treated with depot fluphenazine. In 67 cases, the disease had been present for longer than 5 years. The subjects were administered 25mg of fluphenazine each for 21 days for 3 months to 3 years. Results indicate that while treated with the fluphenazine, 38 subjects demonstrated improvement, 24 showed moderate improvement, and 17 showed mediocre improvement. Some side-effects were discovered, including: sleep disturbances, indifference, anxiety, sadness, and depressive tendencies. It is concluded that depot fluphenazine not only causes clinical improvement but also contributes favorably to the doctor-patient relationship. 19 references. (Journal abstract modified)

003174 Gruzelier, John; Connolly, John; Eves, Frank; Hirsch, Steven; Zaki, Saniha; Weller, Malcolm; Yorkston, Neil. Psychiatry Dept., Charing Cross Hospital Medical School, Fulham Palace Road, London W6 8RP, England **Effect of propranolol and phenothiazines on electrodermal orienting and habituation in schizophrenia.** Psychological Medicine. 11(1):93-108, 1981.

The influence of propranolol and phenothiazines on bilateral electrodermal orienting responses to repeated auditory stimuli was studied with schizophrenic patients and controls. In three studies phasic activity to moderate intensity sounds of patients on no drugs or phenothiazines was predominantly hyperresponsive or hyporesponsive. Controls showed moderate or slow habituation. Propranolol was found to facilitate habituation in slow habituators and to reinstate responses in half of nonresponders, especially when given as the sole drug. The effects seldom had a counterpart in changes in nonspecific responses or levels of skin conductance. It is suggested that modulatory influences on stimulus and response processing and on lateral asymmetries in responses may underlie propranolol's efficacy in treating schizophrenia. 70 references. (Author abstract modified)

003175 Henry, Jean-Francois; Cuche, Henri; Gisselmann, Andre; Zarifian, Edouard; Loo, Henri; Morselli, Paolo L. Dept. de Recherche Clinique, Systeme Nerveux Central, Lers-Synthelabo, 58, rue de la Galciere, F-75013 Paris, France **/GABA and schizophrenia: study of the action of a GABAergic antagonist. Progabide or SL-76002./** GABA et schizophrenie: etude de l'action d'un agoniste GABAergique. Le progabide ou SL 76002. Psychologie Medicale. 12(11):2421-2426, 1980.

The use of progabide or SL-76002 in the treatment of schizophrenia was studied in two open clinical trials. In the first trial, the drug was administered alone to 16 schizophrenic patients (five paranoids, nine hebephrenics, one simple, and one catatonic) for a period of 19 to 60 days at 1800mg/day to 2400mg/day. In the second trial, a group of 10 schizophrenic patients (seven paranoids and three hebephrenics) was administered 1500mg/day to 2200mg/day of the drug in addition to preexisting neuroleptic therapy. Results indicate that the SL-76002 was without therapeutic or antipsychotic effect. Except for sedative effects, the clinical tolerance was good. The results do not support the concept that an increase in GABA activity may be useful in schizophrenia. 17 references. (Journal abstract modified)

003176 Ignatov, S. A.; Burbayeva, G. Sh.; Tsutsul'kovskaya, M. Ya.; Abramova, L. I.; Trubnikov, V. I. Institut psikhiatrii, AMN SSSR, Moskva, USSR **/Beta-endorphin levels in the cerebrospinal fluid of schizophrenics./** Soderzhaniye beta-endorfina v likvore bol'nykh shizofreniyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(9):1331-1337, 1980.

Beta-endorphin levels were studied in the cerebrospinal fluid (CSF) of 24 male schizophrenics and a control group of 15 patients with neurological disorders without the disease syndrome. The Ss included patients with pronounced symptoms of juvenile deteriorating (nuclear) schizophrenia and various forms of juvenile paranoid and attack like progressive schizophrenia, which have a similar course. The Ss were undergoing treatment with psychotropic drugs. During treatment the beta-endorphin levels in the CSF were determined by radioimmune analysis. Treatment was discontinued for 10 days, and the beta-endorphin levels were determined again. Results show a correlation between changes in the beta-endorphin level in the CSF and the patients' clinical state. Reduction in the beta-endorphin level correlates with intensification of hallucinatory/delusional disorders. 26 references. (Journal abstract modified)

003177 Iovchuk, N. M. Pervoye Klinicheskoye otdeleniye Instituta psikhiatrii AMN SSSR, Moskva, USSR /**Late results of lithium treatment of adolescents with attack like schizophrenia.**/ Otdalennyye rezul'taty terapii litiyem podrostkov, bol'nykh pristupoobraznoy schizofreniyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(10):1546-1548, 1980.

Lithium treatment of schizophrenia among children and adolescents was studied in 62 patients (aged 7 to 16 at the beginning of a 9 year period of observation). Lithium therapy was highly effective for 37 of the patients and ineffective for only 12 patients. The group which showed good results had suffered from pronounced affective attacks without a tendency toward protracted unipolar development. In this group, lithium treatment over a long period led to significant reduction in the frequency, length, and severity of attacks, and in some cases to complete disappearance of productive symptoms. The group which showed poor results had suffered from chronic depressive states during puberty and from phased atypical affective disorders leading to an expressed schizophrenic defect. It is concluded that patients whose illness follows this type of course should not be treated with lithium. 8 references. (Journal abstract modified)

003178 Judd, Lewis L.; Janowsky, David S.; Segal, David S.; Parker, Donal C.; Huey, Leighton Y. Dept. of Psychiatry (M-003), University of California at San Diego, La Jolla, CA 92093 **Behavioral effects of methadone in schizophrenic patients.** American Journal of Psychiatry. 138(2)243-245, 1981.

Initial data are reported from a placebo controlled double-blind investigation of the effects of methadone on the behavior of six schizophrenic patients. No significant baseline differences were noted between methadone and placebo days. Methadone produced a small but definite motor slowing and promoted lethargy, deactivation, and loss of function. Negative schizophrenic symptomatology (emotional withdrawal, motor retardation, and blunted affect) increased after methadone administration. An increase in prolactin was noted, probably due to the mediation by the brain of opiate receptors that inhibit dopamine release from the tuberoinfundibular dopaminergic neurons. The data also suggest that methadone hydrochloride does not exert a specific antipsychotic effect in schizophrenic patients but instead accentuates emotional withdrawal and decreases motor activity. 12 references.

003179 Kawahara, Ryuzo; Hazama, Hidebumi; Fukuhara, Tomokazu; Takeshita, Hisayoshi. Dept. of Neuro-psychiatry, Tottori University School of Medicine, Yonago 683, Japan **Biological effects of chlorpromazine in chronic schizophrenics. III. The mutual relation of each index.** Kyushu Neuro-Psychiatry. 26(1):127-134, 1980.

The correlations among physiological and neurochemical indicators were studied in connection with the effects of chlorpromazine on chronic schizophrenics. Ss were 11 schizophrenics, 8 normal chlorpromazine cases, and 5 normal physiological saline cases. The blood prolactin secretion accelerated after chlorpromazine injection and responded to chlorpromazine with shorter latency than that of growth hormone. In schizophrenics, both the appearance percentage of total sleeping time and the systolic blood pressure showed significant correlations with growth hormone secretion after chlorpromazine injection, schizophrenics' systolic blood pressure after chlorpromazine injection showed a paradoxical response as compared to the normal chlorpromazine group; and schizophrenics' heartrate and finger plethysmographic responses to chlorpromazine were almost the same as those of the normal chlorpormazine group. On the basis of the results, the etiology of schizophrenics is discussed in terms of dopaminergic neuronal hypersensitivity, serotoninergic neuronal hyperactivity, and also the vulnerability of the hypothalamus. 28 references. (Author abstract modified)

003180 Kinney, Michael J.; Varga, Ervin; Varga, Vera; Tarter, Ralph; Sugerman, A. Arthur; Nilsen, Stephanie; Gupta, Giriwarlal. Suite 909, 1st Huntington Building, Huntington, WV 25701 **Hemoperfusion for chronic schizophrenia: preliminary psychiatric results.** Journal of Clinical Psychiatry. 42(2):175-178, 1981.

Six patients with chronic schizophrenia unresponsive to accepted therapy were assigned randomly to receive as adjunctive therapy either weekly coated charcoal hemoperfusion (CCHP) or sham hemoperfusion (Sham HP) in a double-blind study using two independent psychiatric raters. Four weeks of treatment suggested that: 1) CCHP was associated with significant improvement in some psychiatric measures; 2) improvement was early in the treatment course; and 3) neither CCHP nor Sham HP was associated with deterioration in any of the psychiatric measures. When one patient from each group was crossed-over to receive the opposite treatment these conclusions were supported. It is concluded that further studies are warranted. 21 references. (Author abstract)

003181 Kurland, Albert A.; Nagaraju, Arramraju. Maryland Psychiatric Research Center, Institute of Psychiatry, School of Medicine, University of Maryland, Baltimore, MD 21201 **Viloxazine and the depressed schizophrenic -- methodological issues.** Journal of Clinical Pharmacology. 21(1):37-41, 1981.

Schizophrenic patients with depressive symptoms were treated with viloxazine or placebo combined with chlorpromazine or haloperidol. No difference between viloxazine and placebo treated groups was found. Since no side-effects were associated with viloxazine, it is possible the doses used were inadequate. 30 references. (Author abstract modified)

003182 Kurland, Albert A.; Nagaraju, Arramraju; Hanlon, Thomas E.; Wilkinson, Edwina H.; Ng, Kung-Tat. Maryland Psychiatric Research Center, Dept. of Psychiatry, School of Medicine, University of Maryland, Baltimore, MD 21201 **A comparison of dopamine receptor blocking assay with plasma drug levels of haloperidol in schizophrenic patients.** Journal of Clinical Pharmacology. 21(1):42-47, 1981.

Biological and chemical assays were used to study plasma neuroleptic levels in seven schizophrenic patients on a fixed dose of haloperidol (20mg/day). Results of the dopamine receptor blocking assay (DRBA) were highly correlated with those obtained by gas chromatography/mass spectrometry. It is suggested that the DRBA could be used to monitor drug compliance, adjust dosage, and evaluate the effects of combined drug treatments. 15 references. (Author abstract modified)

003183 Lindberg, Dick. Dept. II, Lillhagen Hospital, Hisings Backa, Sweden **Management of schizophrenia: long-term clinical studies with special reference to the combination of psychotherapy and depot neuroleptics.** Acta Psychiatrica Scandinavica. 63(Suppl. 289):1-112, 1981.

Results after long-term treatment of schizophrenia were examined with emphasis on the combination of psychotherapy, including other psychosocial treatments, and continuous depot neuroleptic medication, and on building a treatment model for the rehabilitation of schizophrenics. A first sample of younger, male, chronic schizophrenics treated for 5 years with a combination of intensive psychotherapy and depot neuroleptics was significantly changed in a direction indicative of improvement as measured by the Holtzman and Rorschach tests, and is compared with a control group treated with neuroleptics only. A second sample treated with either fluphenazine decanoate or pipothiazine palmitate and studied for 3 years was found to have maintained a low degree of symptoms and signs. A third sample treated according to an integrated treatment model also showed a low level of signs and symptoms. It is noted, however, that although the level of psychopathology was low, difficulties in coping with emotional and practical problems in social life were observed. 158 references. (Author abstract modified)

003184 Luchins, D. J.; Gillin, J. C.; Wagner, R. L.; DeLisi, L. E.; Morihisa, J. M.; Weinberger, D. R.; Bigelow, L. B.; Klein, S. T.; Wyatt, R. J. Adult Psychiatry Branch, Div. of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC **Piperidone in chronic schizophrenic patients: a controlled double-blind study.** Biological Psychiatry. 16(1):91-95, 1981.

In a controlled double-blind study, the effects of piperidine were investigated in five male (one of whom failed to complete the study) and one female schizophrenia inpatients. Ss were started on a 300mg/day dose, increased over 2 weeks to 1600 to 1800mg/day and held constant for 1 month, then increased to 3000 to 3200mg/day and held constant for 1 month. A 3 week placebo period preceded and followed the experimental protocol. No significant drug effect was found to Brief Psychiatric Rating Scale total score or for the six symptom clusters of thought disorder, withdrawal, hostility/suspiciousness, anxiety, depression, or activation for the group or for any patient. No hematological or biochemical changes were associated with the drug period. The only side-effects were nausea and vomiting in one patient and nausea in another at the 3200mg dose; both effects subsided when the dose was reduced. 14 references.

003185 Madruga, Wanderlei Saraiva; Noguiera, Alexandre Barbosa; Costa-e-Castro, Marcelo. Rua Petit Carneiro, 768, 80000 Curitiba, Brazil **/Neuroleptics administered in high dosages./** Neurolepticos em altas doses. Jornal Brasileiro de Psiquiatria. 29(2):99-102, 1980.

The administration of neuroleptics in high dosages to schizophrenic patients is discussed. High doses of these types of drugs represent an alternative for the treatment of chronic schizophrenics resistant to conventional therapeutic measures. The most frequent side-effects experienced with high doses are lethargy and sleepiness; extrapyramidal effects are more frequent with conventional doses. Although high doses have not been found to be superior to the conventional doses until now, it is known that haloperiodol in high doses is efficient in the management of psychomotor agitation. 14 references. (Journal abstract modified)

003186 Manos, Nikolas; Gkiouzepas, John; Logothetis, John. Karolou Diehl 20, Thessaloniki, Greece **The need for continuous use of antiparkinsonian medication with chronic schizophrenic patients receiving long-term neuroleptic therapy.** American Journal of Psychiatry. 138(2):184-188, 1981

A group of 98 chronic schizophrenic patients receiving long-term neuroleptic treatment and trihexyphenidyl were switched to either placebo or study trihexyphenidyl in a double-blind 6 week study. Fifty one (68%) of the 75 Ss given placebo versus one of 23 Ss who continued on active trihexyphenidyl developed severe worsening of extrapyramidal signs, necessitating early termination. Twenty one (28%) of the placebo versus two (8.7%) of the trihexypenidyl Ss developed less severe worsening. Furthermore 50 (66.6%) of the placebo patients, but only two (8.7%) of the trihexyphenidyl Ss had psychotic or other severe physical symptoms related to withdrawal of prestudy antiparkinsonian medication. These data support the need for continuous use of antiparkinsonian medication in the long-term neuroleptic therapy of chronic schizophrenic patients. 20 references. (Author abstract modified)

003187 Matsukura, S.; Yoshimi, H.; Sueoka, S.; Chihara, K.; Fujita, T.; Tanimoto, K. Third Division, Dept. of Medicine, Kobe University School of Medicine, Ikuta-ku, Kobe 650, Japan **Beta-endorphin in Cotard's syndrome.** Lancet. No. 8212:162-163, 1981.

Radioimmunoassays of beta-endorphin and other hormones were conducted in a 41-year-old patient with chronic schizophrenia and Cotard's syndrome. Tests conducted 1 week after withdrawal of neuroleptic medication indicated normal beta-endorphin levels in blood and CSF, similar to those reported for chronic schizophrenics. This suggests that beta-endorphin plays a minor role in schizophrenia and also in analgesia in Cotard's syndrome. Following intravenous administration of 10mg naloxone, no significant changes in hormone levels or in the perception of painful stimuli were observed. On the other hand, naloxone has been reported to increase adrenocorticotropic hormone, luteinizing hormone, and follicle stimulating hormone (without effect on growth hormone, prolactin, or thyroid stimulating hormone) in normal Ss, and has restored pain sensation in congenital insensitivity to pain. 11 references.

003188 May, Philip R. A.; Van Putten, Theodore; Jenden, Donald J.; Yale, Coralee; Dixon, W. J. V.A. Medical Center, Wilshire and Sawtelle Boulevards, Los Angeles, CA 90073 **Chlorpromazine levels and the outcome of treatment in schizophrenic patients.** Archives of General Psychiatry. 38(2):202-207, 1981.

Plasma and saliva levels of chlorpromazine hydrochloride were measured by gas chromatographymass spectrometry, after a standard dosage had been administered to 48 newly admitted schizophrenics over 28 days. Other treatments were rigorously controlled. Saliva chlorpromazine concentrations were higher than plasma concentrations, generally by about four to 50 times. Saliva and plasma chlorpromazine levels were significantly related. There was great variability in individuals between plasma and saliva peaks and values over time, in plasma/saliva ratios, and in change in plasma/saliva ratio over time. chlorpromazine plasma and saliva levels at the end of fixed, sustained dosage treatment did not correlate with amount of improvement as measured by 10 criteria from the Brief Psychiatric Rating Scale and the Mobility, Affects Cooperation, and Communication Scale. Yet, levels obtained in the first 24 hours after the first dose did seem related to outcome, more strongly for saliva chlorpromazine than for plasma chlorpromazine levels. A reexamination of the relationships between levels of antipsychotic drugs in the body and treatment effect is recommended. 32 references. (Author abstract)

003189 May, Philip R. A.; Van Putten, Theodore; Jenden, Donald J.; Yale, Coralee; Dixon, Wilfrid J.; Goldstein, Michael J. V.A. Medical Center Brentwood, 11301 Wilshire Boulevard, Los Angeles, CA 90073 **Prognosis in schizophrenia: individual differences in psychological response to a test dose of antipsychotic drug and their relationship to blood and saliva levels and treatment outcome.** Comprehensive Psychiatry. 22(2):147-152, 1981.

Plasma and saliva chlorpromazine (CPZ) concentrations and their relationships to psychometric change following a single test dose of this antipsychotic drug were studied in a sample of newly admitted schizophrenic patients. There were great individual differences in psychological response: in some, performance was improved; in others, it was reduced. In general, psychometric change followed CPZ plasma levels, but with a definite time lag, and the relationship was neither simple nor direct. There was no significant relationship between test dose performance and the eventual outcome of a course of drug treatment. These observations imply that it is unlikley that there is a simple relationship between therapeutic change and plasma levels. On the basis of results, it is concluded that the most fruitful predictors of therapeutic outcome may be early plasma and saliva levels of drug, early clinical response, and the patient's subjective response to the drug effect. 17 references. (Author abstract modified)

003190 Meltzer, Herbert Y.; Busch, Daniel; So, Rebecca; Holcomb, Henry; Fang, Victor S. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL 60637 **Neuroleptic-induced elevations in serum prolactin levels: etiology and significance.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 149-176).

A series of studies concerning the correlation between serum prolactin levels and clinical improvement in schizophrenic patients after several weeks of neuroleptic treatment is reviewed: specifically, the focus is on what can be learned from pituitary hormone secretion, and on studies related to prolactin and growth hormone secretion. A negative correlation was found between serum prolactin response to a single intramuscular injection of chlorpromazine and clinical response after 1 week of treatment: a possible explanation for this result is proposed which, if correct, would indicate this may be a useful method to identify patients with dopamine (DA) dependent psychoses. Some preclinical endocrine research which sheds new light on the mechanism of action of various psychotropic drugs, including sulpiride, metoclopramide, and LSD, is discussed. It is demonstrated that atypical antipsychotic drugs such as sulpiride and metoclopramide may stimulate prolactin release by a novel mechanism. LSD has been shown to have potent DA-like action at the pituitary, an additional indication that its effects on DA may underlie its psychotomimetic effects. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. 111 references.

003191 Muller, E. Universitats-Nervenklinik mit Poliklinik, Erlangen, West Germany /**Diagnosis and treatment of acute schizophrenic psychoses.**/ Diagnose und Behandlung akuter schizophrener Psychosen. Neurologie und Psychiatrie fur die Praxis. 5:89-91, 1979.

Examples of the onset and symptoms of acute schizophrenic psychoses of various types are presented, and their diagnosis and treatment are discussed. Central emphasis is placed on the danger of the patient's hurting himself or others during paranoid hallucinatory states. The necessity of immediate hospitalization is emphasized, even if it is against the will of the patient or his family. A wide spectrum of manic experiences leading to stupor is illustrated. Therapy with neuroleptics is discussed. (Journal abstract modified)

003192 Okasha, A. Dept. Psychiatrique, Universite Air Shams, Cairo, Egypt /**Carpipramine: a disinhibitory drug compound in chronic schizophrenia.**/ La carpipramine: un compose desinhibiteur dans la schizophrenie chronique. Encephale. 6(2):161-166, 1980.

The use of carpipramine in the treatment of chronic schizophrenics was investigated. Carpipramine was administered orally to 50 subjects in a dosage of 50mg twice daily. The Brief Psychiatric Rating Scale was administered before treatment, after 1 week, 3 weeks and 6 weeks to assess target symptoms. Results indicate that the drug demonstrated a disinhibitory and stimulating effect, with global improvement seen in 70% of the cases; 20% showed no change, and 10% deteriorated owing to exacerbation of psychosis and hyperactivity. Carpipramine was effective in emotional withdrawal, motor retardation, and blunted affect. Residual and pseudoneurotic forms of the illness demonstrated the best response to the drug; onset of response started within 8 to 14 days. The general tolerance, especially compared with last treatment received, was fair. 8 references. (Journal abstract modified)

003193 Petho, B.; Graf, L., Karczag, I.; Bitter, I.; Tolna, J.; Baraczka, K.; Li, Choh Hao. Dept. of Psychiatry, Semmelweis Medical University, H-1038 Budapest, Hungary **Beta-endorphin and schizophrenia.** Lancet. No. 8213:212-213, 1981.

Studies are reported on the beta endorphin treatment of six acute schizophrenic patients in a double-blind design. It was found that beta endorphin affects the temperament, rather than the process symptoms of such patients, and that the results and duration of temperament therapy depends on the nature and symptoms of the psychosis. This interpretation may help resolve discrepancies between other clinical studies. The manner of drug administration may also affect clinical results. 9 references.

003194 Sabbatini, Franco; Lorenzini, R.; Maregha, M. G.; Faore, E. Largo Millefonti, 35, I-10126 Torino, Italy /**The use of a morphine antagonist (naloxone) in the treatment of dissociative syndromes.**/ L'impiego di un antagonista morfinico (naloxone) nel trattamento di sindromi dissociative. Rivista Internazionale di Psicologia e Ipnosi. 20(1):127-131, 1979.

The use of naloxone, a morphine antagonist, in the treatment of dissociative syndromes was studied. Four female patients suffering from dissociative syndromes were administered 0.6mg naloxone the first day and placebo the next 4 days; for 4 more days half the sample received 0.4 naloxone, and the other half received a placebo. Results do not indicate any significant improvement in any of the patients; no difference between naloxone and the placebo was found. 17 references. (Journal abstract modified)

003195 Schooler, Nina R. Psychopharmacology Research Branch, NIMH, Rockville, MD 20857 **Placebo effect: from control to experimental condition.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 389-399).

Methodological issues raised about the design of placebo studies, which need to be addressed if the studies are to be useful, are examined. Several examples are given to suggest that the administration of inert substances can provide information about the biological state of individuals being studied. It is suggested that the understanding of both the positive and negative effects of drugs used in the treatment of schizophrenia makes studies which use placebo treatments innovatively both clinically and ethically appropriate. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. 24 references.

003196 Shalif, Ilan; Lerner, Yakov; Dasberg, Haim. Dasberg: Jerusalem Mental Health Center, Ezrath Nashim, POB 140, Jerusalem, Israel **A symptom profile analysis of antipsychotic drug treatment: nonparametric multidimensional technique.** Psychiatry Research. 4(1):1-12, 1981.

Thirty six schizoaffective patients were treated with haloperidol plus lithium or haloperidol plus placebo. Standard statistical analysis showed greater improvement in those treated with lithium plus haloperidol. The Brief Psychiatric Rating Scale scores were reanalyzed using a nonparametric technique for multidimensional scaling of symptom profiles. The differential outcome after haloperidol with or without added lithium was found to be determined both by symptom dimension and by type of drug. Results show added lithium prevents a depressive shift after haloperidol treatment on the dimension of cognitive disorganization/depressive preoccupation. 11 references. (Author abstract)

003197 Snyder, Solomon H. Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Dopamine receptors, neuroleptics, and schizophrenia.** American Journal of Psychiatry. 138(4):460-464, 1981.

Evidence is presented that the antipsychotic effects of neuroleptic drugs are mediated by dopamine DA-2 receptors and that dopamine DA-1 receptors, linked to cyclic AMP formation, are not involved. Dopamine receptor binding is enhanced in brain specimens of deceased schizophrenic patients, an increase which may relate to chronic neuroleptic treatment. The binding of 3H-butyrophenones to dopamine receptors can be used for a radioreceptor assay that detects blood levels of all clinically used neuroleptics and their pharmacologically active metabolites and may facilitate routine monitoring of blood levels. 31 references. (Author abstract modified)

003198 Tamminga, Carol A.; Tighe, Patti J.; Chase, Thomas N.; DeFraites, E. Gerard; Schaffer, Martin H. Maryland Psychiatric Research Center, PO Box 3235, Baltimore, MD 21228 **Des-tyrosine-gamma-endorphin administration in chronic schizophrenics: a preliminary report.** Archives of General Psychiatry. 38(2):167-168, 1981.

The beta-lipotrophin fragment, des-tyrosine-gamma-endorphin (DTgammaE), which has been reported to have antipsychotic properties, was administered without other psychoactive drugs to a subpopulation of five schizophrenic Ss (three paranoid, two undifferentiated). Male patients with chronic psychotic illness and previous long-term neuroleptic therapy were given DTgammaE at a dose and duration of treatment that have been reported to be effective. No improvement in psychotic symptoms occurred; plasma prolactin level, a parameter characteristically altered by neuroleptic treatment, did not change. The beneficial effects of DTgammaE in schizophrenia may be specific to a diagnostic category, may be dependent on past pharmacological treatment, or may only occur in combination with other drugs. 9 references. (Author abstract modified)

003199 Tune, Larry E.; Creese, Ian; DePaulo, J. Raymond; Slavney, Phillip R.; Snyder, Solomon H. Snyder: Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Neuroleptic serum levels measured by radioreceptor assay and clinical response in schizophrenic patients.** Journal of Nervous and Mental Disease. 169(1):60-63, 1981.

Serum neuroleptic levels and clinical response were compared serially in 10 schizophrenic patients treated with a variety of neuroleptics using a novel radioreceptor assay for neuroleptics. In this assay the drug in serum competes with (3H)spiroperidol for binding to dopamine receptors on membranes of the caudate nucleus. Serum neuroleptic levels, expressed in terms of dopamine receptor occupancy, were similar for most neuroleptics at therapeutic doses. Thioridazine levels were substantially higher than those of other neuroleptics. 24 references. (Author abstract)

003200 Van Praag, H. M.; Verhoeven, W. M. A. Dept. of Psychiatry, University of Utrecht, Utrecht, The Netherlands **Endorphin research in schizophrenic psychoses.** Comprehensive Psychiatry. 22(2):135-146, 1981.

Following a review of the discovery of endorphins and the rationale behind the interest in endorphins in psychiatry, major areas of endorphin research in patients with schizophrenic psychoses are delineated. Reviewed are studies of: 1) endorphins in CSF and dialysate; 2) therapeutic use of opiate (endorphin) antagonists; 3) therapeutic use of endorphins and their derivatives, including studies of beta-endorphin, destyrosine-gamma-endorphin, and FK 33-824, a synthetic met-enkephalin derivative. While the results of such studies have been equivocal, the clinical material is yet too small to warrant definite conclusions. However, therapeutic effects have been reported for these compounds. The most promising findings have been reported for destyrosine-gamma-endorphin, a natural endorphin which lacks morphinomimetic properties and has a number of clinical and pharmacological characteristics in common with the traditional neuroleptics. 46 references.

003201 van Putten, Theodore; May, Philip R. A.; Jenden, Donald J. V.A. Medical Center, Brentwood, CA **Plasma levels of chlorpromazine and clinical response.** Psychopharmacology Bulletin. 17(1):113-115, 1981.

The relationship between plasma levels of chlorpromazine (CPZ) and clinical response was investigated among 34 newly admitted schizophrenic patients treated with 6.6mg/kg CPZ for 28 days. At the end of the fixed dose period, clinical responders had the same plasma levels as nonresponders. This suggests that lack of response is primarily a matter of the illness's sensitivity to CPZ, not to a plasma level below some therapeutic window. Three of the responders had plasma levels greater than 300 picromoles; even though their psychosis responded, all three either appeared overmedicated or complained of side-effects. 1 reference. (Author abstract modified)

003202 Van Putten, Theodore; May, Philip R. A.; Marder, Stephen R.; Wittmann, Lorraine A. V.A. Medical Center, Wilshire and Sawtelle Boulevards, Brentwood, Los Angeles, CA 90073 **Subjective response to antipsychotic drugs.** Archives of General Psychiatry. 38(2):187-190, 1981.

Newly admitted schizophrenic patients (n=63) were given a test dose of thiothixene and their subjective response was recorded by a technician blind to clinical ratings. All patients were then treated with thiothixene in an active milieu setting. Patients varied widely in their subjective responses. An initial dysphoric response was a powerful predictor of both immediate and eventual drug refusal. Before treatment, dysphoric responders tended to be less symptomatic and did significantly better on the Continuous Performance Test. Dysphoric responders experienced significantly more extrapyramidal symptoms following the test dose. Some dysphoric responders did have a good outcome when treated with very low doses. It is recommended that patients with a history of dysphoric response be given a very low dose initially. 17 references. (Author abstract)

003203 Verhoeven, W. M. A.; Van Praag, H. M. Hopital Universitaire, Dept. de Psychiatrie, Nicolaas Beetsstraat 24, Utrecht, The Netherlands /**Endorphins in mental illnesses, and particularly in schizophrenia.**/ Les endorphines dans les maladies mentales, en particulier dans la schizophrenie. Encephale. 6(2):103-113, 1980.

The results of clinical studies with naloxone, beta-endorphin, the synthetic met-enkephalin analogue FK-33-824, and des tyrosine-gamma-endorphin in schizophrenia and other mental illnesses are discussed. The clinical results of treatment of schizophrenia with des tyrosine-gamma-endorphin present the greatest scientific interest. This endogenous neuropeptide, apparently occurring naturally in the brain, has pharmacologic properties similar to those of conventional neuroleptics such as the phenothiazines and butyrophenones. It is thus conceivable that des tyrosine-gamma-endorphin may be an endogenous antipsychotic agent and that its deficiency may contribute to the pathogenesis of certain types of schizophrenia. 42 references. (Journal abstract modified)

003204 Welbel, Leszek. Instytut Psychoneurologiczny Al. Sobieskiego 1/9, 02-957 Warszawa, Poland /**Differences in the clinical action of some neuroleptic drugs.**/ Roznice w dzialaniu klinicznym niektorych neuroleptykow. Psychiatria Polska. 14(2):113-118, 1980.

The effectiveness and clinical properties of six neuroleptics were studied using 118 male and 117 female schizophrenic patients from five psychiatric hospitals. The changes in their mental condition were evaluated by using the Brief Psychiatric Rating Scale. It was found that in cases of chronic schizophrenia the condition of at least 70% of the patients improved substantially. The best results were obtained by using chlorpromazine, methotrimethrazine, trifluoperazine, and clozapine. Differences between the neuroleptics in terms of strength were statistically insignificant. These drugs were found to be somewhat more effective than pimozide and sulpiride. Chlorpromazine and clozapine are more effective in cases of motor disorders and psychosis. Pimozide and sulpiride are indicated for patients suffering from motor disorders accompanied by axial schizophrenic symptoms. Methotrimeprazine is most effective in patients suffering from restlessness accompanied by depression. It is concluded that trifluoperazine has the most balanced clinical profile. 29 references.

003205 Zahn, Theodore P. Laboratory of Psychology and Psychopathology, NIMH, Bethesda, MD 20205 **Predicting outcome from measures of attention and autonomic functioning.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 81-106).

To support the thesis that attention and autonomic nervous system (ANS) activity should be measured more often in clinical studies of schizophrenia, evidence is presented which suggests that attention and ANS functioning may be partly biologically determined traits with etiological and prognostic significance. New evidence is reviewed on: 1) the relationship of measures of attentional and autonomic functioning to subsequent clinical course (that is, outcome) in both unmedicated patients and those taking antipsychotic drugs; 2) changes in psychophysiological functioning in relation to clinical changes -- changes which occur in unmedicated patients are compared to changes attributable to drugs; and 3) other relevant evidence on possible genetic and neurochemical determinants of the attentional ANS deficts in schizophrenia. The data suggest that ANS activity is related to biogenic amines and to enzyme activities which are thought to play important etiological roles in schizophrenia. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. 61 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

003206 Alby, J. M.; Ferreri, M. Dept. de Psychiatrie et de Psychologie Medicale, Hopital Saint-Antoine, 184, rue du Faubourg-Saint Antoine, F-75012 Paris, France /**Clinical study of maprotiline in the treatment of depressive states: compilation of 1520 observations.**/ Etude clinique de la maprotiline dans le traitement des etats depressifs: synthese de 1520 observations. Encephale. 6(2):145-159, 1980.

A new antidepressant, maprotiline, was studied in general practice. A total of 1520 cases, complied by 150 general practitioners and 27 psychiatrists, were evaluated through a questionnaire study. In the majority of cases, the drug was given to outpatients. Results indicate good or excellent improvement with least possible intolerance of mental disorders in 79% of cases. It is concluded that maprotiline is an effective antidepressant, requiring the usual precautions; it is well suited to outpatient treatment of various forms of depression often encountered in daily practice. 42 references. (Journal abstract modified)

003207 Bertolini, Raffaele. Istituto Psichiatrico /**Observations on the use of citicoline in dysthymic patients.**/ Osservazioni sull'impiego della citicolina nelle sindromi distimiche. Rivista Sperimentale di Freniatria. 103(2):406-411, 1979.

The utilization of citicoline in the treatment of dysthymic patients was studied in 30 subjects suffering from depressive diseases. The sample consisted of men aged 18 to 65, who were suffering from endogenous, reactive, senile, and neurotic depression. The first week the subjects were administered 750 to 1000mg of citicoline daily. During the next 3 weeks, the treatment was reduced to 500mg per day. Results show that citicoline in monotherapy is effective only in depressive involutional syndromes. However, it should be added that the use of the drug in association with tricyclic antidepressants causes a less prolonged but more complete recovery of the affective equilibrium. 7 references. (Journal abstract modified)

003208 Blauwblomme, Jean-Francois; Garre, Jean-Bernard; L'Huillier, Jean-Paul; Leguay, Denis; Wartel, Roger. Clinique hospitalo-universitaire, F-49470 Sainte-Gemmes-sur-Loire, France /**Therapeutic trial of a new antidepressant: mianserin.**/ Essai therapeutique d'un nouvel anti-depresseur: la mianserine. Psychologie Medicale. 12(7):1602-1608, 1980.

The use of mianserin in the treatment of depression was studied. Thirty depressed patients of all ages and both sexes were given 10mg of mianserin three times daily for the first week and 20mg three times daily for 3 more weeks. The subjects were evaluated regularly using the Hamilton Depression Scale. Results indicate improvement in the majority (25) of the cases. The drug also demonstrated sedative properties, good tolerance, and few harmful side-effects. 28 references. (Journal abstract modified)

003209 Boldyrev, A. I.; Pozdnyakov, V. S. Klinika epilepsii Moskovskogo NII psikhiatrii Ministerstva zdravookhraneniya RSFSR, Moscow, USSR /**Pathomorphosis of chronic epileptic psychoses.**/ Patomorfoz khronicheskikh epilepticheskikh psikhozov. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(6):829-833, 1980.

The pathomorphosis of chronic epileptic psychoses was studied in 69 patients (age 20 to 60), all of whom were hospitalized at the time of the study. Anticonvulsive treatment combined with neuroleptic drugs was found to hinder the development of such chronic psychoses, but it was unsuccessful in preventing the development of intellectual and personality defects. Although the program of treatment reduced impulsiveness in the patients' behavior, it did nothing to reduce aggressiveness and in some cases aggravated the problem of hallucinations, particularly auditory ones. 14 references. (Journal abstract modified)

003210 Braccini, T.; Darcourt, G. Service de Psychiatrie et de Psychologie Medicale, Hopital Pasteur, F-06031 Nice Cedex, France /**Correlations between lithium levels in cerebrospinal fluid and lithium levels in blood plasma and erythrocytes.**/ Correlations entre la lithorachie et les taux de lithium dans le plasma et dans les erythrocytes. Encephale. 6(2):131-137, 1980.

Correlations between lithium levels in cerebrospinal fluid and in blood plasma and erythrocytes were studied. The lithium levels were measured in 22 patients who had received lithium therapy. Results indicate a greater correlation between levels from plasma and cerebrospinal fluid than between levels from erythrocytes and cerebrospinal fluid. A formula was developed which is used to predict lithium levels in cerebrospinal fluid. It was also found that cerebral organicity did not influence the transmembrane passage of lithium 5 references. (Journal abstract modified)

003211 Brown, Walter Armin; Haier, Richard J.; Qualls, C. Brandon. Providence V.A. Medical Center, Providence, RI **The dexamethasone suppression tes: in the identification of subtypes of depression differentially responsive to antidepressants.** Psychopharmacology Bulletin. 17(1):88-90, 1981.

Studies of the dexamethasone suppression test (DST) in the identification of subtypes of depressive patients differentially responsive to antidepressants are described. Preliminary results suggest that the DST identifies two subgroups of depression which differ in course of illness and in early treatment response. It is reported that nonsuppressors with primary depression are older than suppressors. Neurochemical data indicate that imipramine and desipramine are likely to have greater in vivo effects on noradrenaline uptake and lesser effects on serotonin uptake than clomipramine and amitriptyline. The apparent preferential response among nonsuppressors to desipramine and imipramine, along with data suggesting tonic noradrenergic inhibition of the pituitary/adrenal system, raises the speculation that depressed patients with nonsupression have a functional deficiency in central noradrenergic transmission. 7 references. (Author abstract modified)

003212 Burten, William; Ballard, Bruce L. Dept. of Psychiatry, New York Hospital-Westchester Div., Cornell University Medical College, 21 Bloomingdale Rd., White Plains, NY 10605 **Hypomania as a stable state: lithium prophylaxis in two patients.** American Journal of Psychiatry. 138(4):523-524, 1981.

Two case reports are presented on the successful treatment of two patients with hypomania through a procedure which titrated lithium to maintain the patients at a functional level. The patients continued to be hypomanic but were able to work steadily and maintained object relations on an acceptable social level for more than 5 years. Such a treatment approach is recommended for the small number of bipolar affective disordered patients who might otherwise stop their medication because they miss the euphoria associated with chronic mood elevation and who are capable of functioning well at a hypomanic level. 7 references.

003213 Claghorn, James L.; Mathew, Roy J. Texas Research Institute of Mental Sciences, Houston, TX **Clinical trials with new bicyclic and tetracyclic compounds: zimelidine and maprotiline.** Psychopharmacology Bulletin. 17(1):23-26, 1981.

Clinical trials with new bicyclic and tetracyclic compounds (zimelidine and maprotiline) are reviewed, and the biochemical events underlying depressive states are discussed. The paradox of the clinical effectiveness of two agents with such different effects (zimelidine, a potent serotonin (5-HT) reuptake inhibitor; and maprotiline, a comparatively specific inhibitor of the nonrepinephrine (NE) system) is discussed in relation to various clinical trials of these agents. It is concluded: 1) that animal models are inappropriate, as the neurochemical derangements demonstrated in depressed humans are not present in animals; 2) that the tricyclic antidepressants (TCA) share a mechanism in common which is independent of NE or 5-HT effects such as the induction of subsensitivity of NE stimulated adenyl cyclase; and 3) that results of acute animal experiments may not reflect effects resulting from chronic treatment with TCAs. 8 references. (Author abstract modified)

003214 Coleman, James H.; Johnston, Joseph A.; Callaway, Janice T.; May, Charles N.; Druff, James H. Pharmacy Dept., V. A. Hospital, 1030 Jefferson, Memphis, TN **Protocols for the use of psychoactive drugs -- Part II: protocol for the treatment of depression with tricyclic antidepressants.** Journal of Clinical Psychiatry. 42(2):65-68, 1981.

In the second in a series of protocols for the use of psychoactive drugs, a stepwise decision-making process is presented for the treatment of depression with tricyclic antidepressants. The 39 step protocol traces patient management from the initial diagnosis of depression through assessment of treatment response and drug related problems (side-effects, dose adjustment, alternative medication), through followup of continuing treatment and yearly psychiatric reexamination. 14 references.

003215 Davis, Bonnie M.; Pfefferbaum, Adolf; Krutzik, Siegfried; Davis, Kenneth L. Special Diagnostic and Treatment Unit, V.A. Medical Center, 130 West Kingsbridge Rd., Bronx, NY 10468 **Lithium's effect on parathyroid hormone.** American Journal of Psychiatry. 138(4):489-492, 1981.

Changes in serum calcium and serum phosphate concentrations and of urinary calcium excretion which may be attributable to parathyroid hormone (PTH) in lithium treated psychiatric patients were investigated. PTH was measured in 18 depressed patients receiving lithium, and it was significantly higher in these Ss than in 150 normal Ss. For all patients, serum calcium concentrations correlated significantly with serum lithium concentrations. These results indicate that lithium may cause biochemical hyperparathyroidism. Secondary hyperparathyroidism in certain patients with lithium nephrotoxicity is also possible. 14 references. (Author abstract modified)

003216 de Cuyper, Hugo J. A.; van Praag, Herman M.; Mulder-Hajonides, Wilhelmina R. E. M.; Westenberg, Herman G. M.; de Zeeuw, Rokus A. Westenberg: Dept. of Psychiatry, Academic Hospital Catharijnesringel 101, Utrecht, Netherlands **Pharmacokinetics of clomipramine in depressive patients.** Psychiatry Research. 4(2):147-156, 1981.

Ten patients with a vital depressive syndrome were treated for 4 weeks with clomipramine (CI), five receiving the drug by mouth and five receiving it first intramuscularly (i.m.) and then by mouth. Plasma concentrations of CI and desmethylclomipramine (DCI) were measured daily. Both concentrations showed marked interindividual differences, especially after oral administration of the drug. The mean relative CI clearance after repeated i.m. injections was .441kg-1hour-1. The route of administration proved to exert a marked influence on the plasma concentration ratio CI/DCI. In this small population, no significant relationship could be demonstrated between plasma CI and DCI concentrations, or the sum of both, and clinical effect. 15 references. (Author abstract)

003217 Donlon, Patrick T.; Biertuemphel, Hugo, III; Willenbring, Mark. Suite 274, 601 University Ave., Sacramento, CA 95825 **Amoxapine and amitriptyline in the outpatient treatment of endogenous depression.** Journal of Clinical Psychiatry. 42(1):11-15, 1981.

In a double-blind investigation the onset of action, the efficacy, and the safety of amoxapine and amitriptyline were compared in 46 endogenously depressed outpatients. Statistical analysis demonstrated relatively few significant differences in improvement between the two groups. Most of the differences favored amoxapine, however, and on all measures there were clear trends favoring amoxapine for more rapid onset of action or greater overall efficacy or both. 17 references. (Author abstract)

003218 Emrich, H. M.; von Zerssen, D.; Kissling, W.; Moller, H.-J.; Windorfer, A. Max-Planck Institut fur Psychiatrie, Kraepelinstr. 10, D-8000 Munchen 40, West Germany **The effect of sodium valproate on mania: the GABA-hypothesis of affective disorders.** Archiv fur Psychiatrie und Nervenkrankheiten. 229(1):1-16, 1980.

A possible antimanic property of the GABAergic anticonvulsant valproate was examined by use of a double-blind placebo controlled ABA design in five acutely ill manic patients. In four cases a marked improvement was observed after valproate medication, whereas one patient showed no response. Seven further patients with frequently recurring episodes of a manic or maniform schizoaffective psychosis, irresponsive to lithium prophylaxis, were chronically treated with valproate in combination with low doses of lithium (one case only with valproate). Over an observation period of 1.5 to 3 years none of the patients exhibited a relapse. It is proposed that, in general, GABAergic anticonvulsants possess antimanic properties and that the specific antimanic effect of lithium is due to a GABAergic mode of action. The possible role of GABA systems in affective disorders and in organic types of psychoses is considered. 59 references. (Author abstract modified)

003219 Emrich, H. M.; von Zerssen, D.; Kissling, W.; Moller, H. -J. Max-Planck-Institut fur Psychiatrie, D-8000 Munchen 40, West Germany **On a possible role of GABA in mania. Therapeutic efficacy of sodium valproate.** Advances in Biochemical Psychopharmacology. 26:287-296, 1981.

The therapeutic value of sodium valproate in manic psychoses was investigated in two studies: 1) a placebo controlled, double-blind, ABA design with acutely manic inpatients; and 2) an open trial, with prophylactic long-term treatment of lithium nonresponders (outpatients). Results strongly suggest that valproate is a promising candidate for use in treatment of manic syndromes, since the dosage range required for its prophylactic and acute effects upon mania is in the same range as in the pharmacotherapy of epileptic disorders, and since side-effects are rare. Results are consistent with the hypothesis that activation of the GABA system may produce antimanic effects. Clinical implications are noted. 31 references.

003220 Extein, Irl; Pickar, David; Gold, Mark S.; Gold, Philip W.; Pottash, A. L. C.; Sweeney, Donald R.; Ross, Richard J.; Rebard, Robert; Martin, David. Fair Oaks Hospital, Summit, NJ **Methadone and morphine in depression.** Psychopharmacology Bulletin. 17(1):29-33, 1981.

The effects of single doses of methadone and morphine on clinical depression and neuroendocrine response were investigated in two experiments. The first study was an open investigation in 10 inpatients with major depressive disorder (defined by research diagnostic criteria; the second study was a double-blind, placebo controlled study of 6 depressed inpatients. Despite the lack of clear clinical antidepressant effects of single doses of opioids, the neuroendocrine results suggest dysfunction in central endorphin systems in depression. 10 references. (Author abstract modified)

003221 Fieve, Ronald R.; Meltzer, Herber L.; Dunner, David L.; Fleiss, Joseph L. New York State Psychiatric Institute, 722 West 168th Street, New York, New York 10032 /**The repression of the response to prophylactic treatment.**/ La represion del litio respuesta al tratamiento profilactico. Actas Luso-Espanolas de Neurologia, Psiquiatria etc. 8(3):205-210, 1980.

The lithium content in erythrocytes and plasma of patients suffering from depression was studied. Lithium pumps, the active interchange of lithium between cells and intercellular space, were obtained in 69 depressive patients over a period of 24 months. Results indicate no significant differences between subjects who responded well or badly to treatment with respect to age, sex, or lithium content. Those patients with lower lithium flow responded well to prophylactic treatment while continuing their lithium therapy. It is concluded that lithium flow is an index of the capacity of lithium to prevent depression. 12 references.

003222 Frezza, G.; Di Marco, E.; Giuffra, F. Ospedale Psichiatrico Provinciale, Genova-Quarto, Italy /**Nomifensine: considerations on a new nontricyclic antidepressant.**/ Alcune considerazioni su un nuovo antidepressivo non triciclico: il nomifensine. Rivista Sperimentale di Freniatria. 103(1):193-200, 1979.

The use of a new nontricyclic antidepressant, nomifensine, was studied in 38 subjects with depressive symptomatology. The subjects, 15 men and 23 women, were examined and treated with nomifensine in doses varying from 25 to 250mg daily. The effects of nomifensine were evaluated with Hamilton's Depression Scale. The results indicate that nomifensine is an excellent antidepressant drug, particularly for neuroses and reactive depressive syndromes, and that it is very easy to manage and has few side-effects. 10 references. (Journal abstract modified)

003223 Gawin, Frank H.; Markoff, Richard A. Yale University School of Medicine, 34 Park Street, New Haven, CT 06508 **Panic anxiety after abrupt discontinuation of amitriptyline.** American Journal of Psychiatry. 138(1):117-118, 1981.

Withdrawal symptoms following abrupt discontinuation of amitriptyline are reported in a 29-year-old man admitted to the hospital for depressed mood and suicidal impulses apparently associated with his wife's request for a divorce. At discharge, the patient elected to enter an Alcoholics Anonymous oriented halfway house to qualify for admission; he abruptly discontinued both amitriptyline and disulfiram. He experienced a withdrawal attack 2.5 days later which corresponded to DSM-III criteria for an episode of panic anxiety. Subjective feelings of anxiety and accompanying autonomic signs were relieved by restarting amitriptyline and not by psychological support or oxazepam. Further symptoms recurred when amitriptyline was stopped a second time and again responded to reinitiation of amitriptyline. 9 references.

003224 Georgotas, Anastase; Gershon, Samuel. Dept. of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Historical perspectives and current highlights on lithium treatment in manic-depressive illness.** Journal of Clinical Psychopharmacology. 1(1):27-31, 1981.

A historical review of the use of lithium in the treatment of manic-depressive illness is presented. It is noted that in Roman times physicians first recommended alkaline springs in the treatment of mania. Contemporary interest in lithium began in 1949, with a report of improvement of mania in 10 of 10 patients. Since then, lithium has become increasingly popular both for treating acute mania and as a prophylactic agent. Its use in depression is also described. The clinical spectrum of lithium is discussed, and its use for disorders other than mania is described. 45 references. (Author abstract modified)

003225 Gillis, John S. Oregon State University, Corvallis, OR 97331 **Effects of tricyclic antidepressants on interpersonal learning.** Research Communications in Psychology, Psychiatry and Behavior. 6(1):49-62, 1981.

Three tricyclic antidepressants, amitriptyline, imipramine and doxepin, used alone and in combination with antipsychotics, were compared with regard to their effects on several parameters of interpersonal learning. Fifty depressed inpatients were divided into seven treatment groups based on their existing chemotherapy regimens. Performance was assessed on a series on quantitative indices derived from the learning tasks. Subjects in all treatment conditions performed in a stable, effective manner in marked contrast to patients in previous studies who were receiving neuroleptics and dealing with similar materials. No statistically significant differences were obtained among the tricyclics although the pattern of nonsignificant differences was highly consisistent. amitriptyline subjects, whether receiving supplementary antipsychotic medication or not, performed best on every major index of performance. 20 references. (Author abstract)

003226 Goldberger, E.; Clavere, J. L.; Espagno, J. Hopital de Purpan-Casselardit, F-31052 Toulouse Cedex, France **/Dosage of intratumoral lithium (cerebral glioblastoma): on a failure of treatment of manic-depressive psychosis./** Dosage du lithium intra-tumoral (glioblastome cerebral): a propos d'un echec du traitement d'une psychose maniaco-depressive. Encephale. 6(2):139-144, 1980.

A case of cyclothymia in a 49-year-old man in a subacute manic phase treated by lithium carbonate is described. Lithium therapy failed to reverse the cyclothymia, although a valuable blood level of lithium was achieved. Upon discovery of a brain tumor, unaccompanied by neurological or psychological symptoms, neurosurgery was performed which showed a right centromedial cerebral glioblastoma. A biopsy revealed high intracellular level of lithium with a high ratio of cell to blood levels. It is postulated that the cells of the brain tumor have a special affinity for lithium, depriving the normal tissue by competition. This would explain the sudden failure of lithium therapy. 13 references. (Journal abstract modified)

003227 Halaris, Angelos E.; Stern, Warren; Harto-Truax, Nancy. Veterans Administration Hospital, Brentwood, CA **Clinical efficacy of the new antidepressant bupropion (Wellbutrin).** Psychopharmacology Bulletin. 17(1):140-142, 1981.

The efficacy and safety of bupropion, a compound remotely related to catecholamines, in the treatment of depression were investigated in a double-blind, placebo controlled study. Results clearly demonstrate that bupropion is significantly more effective than placebo in controlling the symptoms of depression. The response rate among the 21 patients studied was about 60%, which is comparable to the response rate generally obtained with tricyclic antidepressants. Bupropion appears to possess anxiolytic activity when anxiety symptoms accompany the depressive syndrome. However, the rate of improvement of the anxiety symptoms is slower than that of depression. 2 references.

003228 Halbreich, Uriel; Weinberg, Uzi; Stewart, Jonathan; Klein, Donald F.; Weitzman, Elliot D.; Quitkin, Frederic M. Dept. of Psychiatry, Montefiore Hospital and Medical Center, 111 E. 210th St., Bronx, NY 10467 **An inverse correlation between serum levels of desmethylimipramine and melatonin-like immunoreactivity in DMI-responsive depressives.** Psychiatry Research. 4(1):109-113, 1981.

The relationship between plasma levels of the tricyclic antidepressant desmethylimipramine (DMI) and plasma levels of melatonin like immunoreactivity was studied in 32 endogenously depressed patients. An inverse correlation between plasma levels of DMI and plasma levels of melatonin, like immunoreactivity was found in the group of clinical responders to the chronic administration of the drug. The nonresponders had higher levels of melatonin like immunoreactivity at comparable levels of DMI. This finding is consistent with the hypothesis that chronic high plasma levels of DMI may down regulate the beta-adrenergic receptors in man; however, some other homeostatic mechanisms may be involved in the clinical response. 24 references. (Author abstract)

003229 Harrison-Read, P. E. Dept. of Pharmacology, Medical College of St. Bartholomew's Hospital, Charterhouse Square, London EC1M 6BQ, England **Synaptic and behavioural actions of antidepressant drugs: further thoughts on the implications for theories of depression.** Trends in NeuroSciences. 4(2):32-34, 1981.

Research strategies for determining the synaptic and behavioral actions of antidepressant drugs are evaluated. By reflecting the integrated functioning of neural systems, behavioral studies can reveal the net effect on noradrenergic transmission of various presynaptic and postsynaptic changes which potentially could alter transmission in opposite directions. A similar case can be made for the value of electrophysiological studies of cells receiving noradrenergic input. Studying the integrated function of noradrenergic systems during long-term drug administration may also help in distinguishing primary effects of drugs on synaptic functions from adaptive or compensatory changes occurring secondarily, and may be particularly relevant to antidepressant effects. Topics discussed include: effects of tricyclic antidepressants on noradrenergic systems; antidepressants and information transfer; antidepressants and lithium as stabilizers of monoaminergic transmission; and a permissive monoamine hypothesis of depression. 27 references.

003230 Hugonenq, H.; Uso, T. Barnetil, Laboratoire Delagrange, Marseille, France **/On the effects of sultopride administered in low dosages to older children and adolescents./** A propos de l'interet du sultopride utilise a faibles doses chez le grand enfant et l'adolescent. Neuropsychiatrie de l'Enfance et de l'Adolescence. 28(12):593-597, 1980.

The effects of sultopride administration in low dosages to 15 psychotic patients between ages 10.5 and 17 were studied. Diagnoses included psychoaffective disorders, paranoid psychosis, early childhood psychosis, dissociative psychosis, early infantile autism, epileptic psychosis, and characterological disorders. The object of treatment was to suppress, or at least partially reduce, symptoms of instability, aggressiveness, delirium, and other pathological manifestations responsible for maladjusted behavior. Dosages between 15mg and 60mg daily (corresponding to 0.5 to 1mg/kg/day) were administered for an average duration of 1 month. The results show that sultopride caused some motor relaxation, which increased the effectiveness of psychotherapeutic treatment. Side-effects were common, however.

003231 Jessel, H. J.; Jessel, I.; Seeler, W. Allgemeines Krankenhaus, Hamburg, West Germany **/Double-blind study of mianserin and amitriptyline./** Doppelblindstudie zwischen Mianserin und Amitriptylin. Neurologie und Psychiatrie fur die Praxis. 5:262-264, 1979.

In a double-blind study, mianserin and amitriptyline were compared for their antidepressant effects. Overall clinical impressions and Beck's self-evaluation scale were the test measures employed. Despite obvious similarities as antidepressants, mianserin had fewer side-effects. Furthermore, no marked hematological or other chemical changes were found during the treatment with mianserin. (Journal abstract modified)

003232 Kabes, J. Ustavni 91, 180 00 Praha 8, Czechoslovakia / **Combined administration of nialamide and viloxazine to depressive patients.**/ Kombinovane podavani nialamidu a viloxazinu u depresivnich nemocnych. Ceskoslovenska Psychiatrie. 75(3):166-174, 1979.

The effect of successive and combined treatment of depression with viloxazine and nialamide was studied. It was found that the drugs get a very good therapeutic response, undesirable reactions are reduced to a minimum, and no symptoms of toxicity are observed. Viloxazine seems to be the drug of choice for overcoming the therapeutic gap between the administration of monoamine oxidase inhibitors (MAOI) and tricyclic antidepressants, or vice versa. It is concluded that combined administration of MAOI and viloxazine could be an effective therapeutic treatment for depressions which resist the classic antidepressive treatment presently available. 17 references. (Journal abstract modified)

003233 Kane, John M.; Quitkin, Frederic M.; Rifkin, Arthur; Ramos-Lorenzi, Jorge R.; Saraf, Kishore; Howard, Alfreda; Klein, Donald F. Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Prophylactic lithium with and without imipramine for bipolar I patients: a double-blind study.** Psychopharmacology Bulletin. 17(1):144-145, 1981.

The value of adjunctive imipramine in lithium treated bipolar manic-depressive illness was investigated. In a double-blind study, 37 patients were randomly assigned to lithium plus imipramine and 38 to lithium and placebo imipramine. Because depressive relapse rates were so low in both groups, the advantage of adding imipramine to a lithium prophylactic regime could not be demonstrated. On the other hand, there was little evidence that the combination of lithium and imipramine caused adverse reactions with the possible exception of a subgroup of female or mania prone patients. 4 references.

003234 Kaumeier, H. S.; Haase, H. J. Kalmusweg 11, D-6701 Neuhofen, West Germany **A double-blind comparison between amoxapine and amitriptyline in depressed in-patients.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 18(4):177-184, 1980.

The effects of amoxapine (mean total daily dose, 147.5mg) were compared with those of amitriptyline (mean total daily dose, 152.5mg) in a 6 week double-blind study of 50 depressed inpatients. Amoxapine appeared to be superior to amitriptyline on the basis of scores on the Hamilton Psychiatric Rating Scale for depression, Beck Depression Inventory Short Form, Nurses Observational Scale for Inpatient Evaluation, Clinical Global Impression, Patient Self-Evaluation Scale, and other quantitative assessments. Amoxapine also showed earlier onset of action than amitriptyline. The incidence of side-effects was comparable in the two groups. 3 references. (Author abstract modified)

003235 Kovacs, Maria; Rush, A. John; Beck, Aaron T.; Hollon, Steven D. Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Depressed outpatients treated with cognitive therapy or pharmacotherapy: a one-year follow-up.** Archives of General Psychiatry. 38(1):33-39, 1981.

Using a controlled, clinical trial format, 44 nonpsychotic, nonbipolar, depressed outpatients were treated with cognitive therapy or imipramine hydrochloride over a 12 week period. Although both interventions were associated with significant reductions in levels of depression, the cognitive therapy patients showed greater symptomatic improvement and a higher treatment completion rate. A 1 year naturalistic followup of the 35 subjects who completed the protocol revealed that although many of the patients had a variable clinical course, both original treatment groups remained generally well. Self-rated depressive symptomatology was significantly lower for those who, 1 year earlier, had completed cognitive therapy than for those who had been in the clinical trial's pharmacotherapy cell. While there were several other interesting trends in favor of the cognitive therapy patients, none of the between group differences were significant. The pragmatic and clinical implications of the followup results are discussed. 27 references. (Author abstract)

003236 Kupfer, David J.; Spiker, Duane G.; Coble, Patricia A.; Neil, John F.; Ulrich, Richard; Shaw, David H. Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Sleep and treatment prediction in endogenous depression.** American Journal of Psychiatry. 138(4):429-434, 1981.

The use of psychobiological measures to increase the accuracy of clinical prediction in primary endogenous depression was assessed in 34 patients. Ss were treated with amitriptyline and EEG monitored sleep criteria were applied. Such criteria were more significant than clinical status alone in predicting clinical response. Prolonged REM latency and reduced difficulty in sleep onset following the administration of amitriptyline were the main sleep variables contributing to this prediction equation. The data suggest a strong relationship between clinical outcome and psychobiological profile in patients with endogenous depression after a pharmacological probe with a tricyclic antidepressant. 24 references. (Author abstract modified)

003237 Linkowski, P.; Brauman, H.; Mendlewicz, J. Mendlewicz: Dept. of Psychiatry, Hospital Erasme, Free University of Brussels, 808 Route de Lennick, B-1070 Brussels, Belgium **Thyrotrophin response to thyrotrophin-releasing hormone in unipolar and bipolar affective illness.** Journal of Affective Disorders. 3(1):9-16, 1981.

The plasma levels of thyrotrophin (TSH) and the response of this hormone to 200 mcg of thyrotrophin releasing hormone (TRH) were studied in 27 unipolar and 24 bipolar depressed females before and after amitriptyline treatment, as well as in 42 normal controls. No significant differences were noted in basal TSH levels when groups were studied according to diagnosis, menopausal status and antidepressant treatment. After amitriptyline treatment, the TSH response to TRH, which was impaired before treatment in bipolar premenopausal Ss, improved significantly. No significant differences as a function of treatment could be demonstrated in unipolar postmenopausal Ss in whom TSH response was blunted before treatment. The findings suggest that the differential TSH response to TRH in unipolar and bipolar patients may constitute biological markers of endocrine dysfunction in clinical subgroups of affective disorders. 21 references. (Author abstract modified)

003238 Lloyd, Camille; Zisook, Sidney; Click, Maurice, Jr.; Jaffe, Kenneth E. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical School, Houston, TX **Life events and response to antidepressants.** Journal of Human Stress. 7(1):2-15, 1981.

The relationship of life-events and response to tricyclic antidepressants was examined among 80 outpatients with unipolar, primary depressions. Participants were randomly assigned to receive either amitriptyline or amoxapine. Events occurring in either the 2 or 12 months prior to starting treatment (antecedent events) were unrelated to antidepressant response. However, events occurring during the treatment period itself (concurrent events) were significantly related to tricyclic response. Patients evidencing the poorer response reported almost three times as many concurrent events as the more improved patients. A poorer tricyclic response was associated in particular with concurrent events which were undesirable, health related, and perceived as being outside of the patient's own control. It is suggested that the continuing occurrence of stressor events probably interferes with treatment efforts and, therefore, it may be important for the therapist to pay careful attention to the ongoing life stresses of the depressed patient. 31 references. (Author abstract)

003239 Logue, James N.; Sachais, Barry A. GEOMET Technologies, Inc., Rockville, MD **Factors which affect antidepressant drug response in a multicenter controlled trial.** Psychopharmacology Bulletin. 17(1):138-139, 1981.

Factors which affect antidepressant drug response were studied via analysis of data from a multicenter trial which compared a new tetracyclic antidepressant, maprotiline, with imipramine in the treatment of severe depression. Four pretreatment characteristics of the 231 Ss were investigated: age, global severity of illness, weeks since onset of current episode, and pretreatment level of anxiety. Results indicate that maprotiline, a specific norepinephrine reuptake inhibitor, is preferentially effective with younger patients, more severely depressed patients, and those who have a relatively recent onset of the current episode. 5 references.

003240 McGrath, Patrick J.; Quitkin, Frederick, J.; Stewart, Jonathan W.; Leibowitz, Michael; Fyer, Abby; Davies, Sharon; Klein, Donald F. New York State Psychiatric Institute, New York, NY **Novel antidepressants: a clinical trial of mianserin.** Psychopharmacology Bulletin. 17(1):21-23, 1981.

A clinical trial of a novel tetracyclic antidepressant, mianserin, with a sample of patients who met research diagnostic criteria for major depressive disorder is described. Clinical response was steady and progressive with continuing improvement up to 6 weeks of active drug therapy. This suggests that maximum improvement requires at least 6 weeks of treatment, and/or a dose of 150mg/day. Mianserin's efficacy is shown to approximate that of tricyclic antidepressive drugs. Its low incidence of side-effects and apparent high margin of safety make it a useful addition to the psychopharmacologic armamentarium. 9 references. (Author abstract modified)

003241 McGrath, Patrick J.; Quitkin, Frederick M.; Stewart, Jonathan W.; Liebowitz, Michael; Fyer, Abby; Davies, Sharon. 722 West 168th St., New York, NY 10032 **An open clinical trial of mianserin.** American Journal of Psychiatry. 138(4):530-532, 1981.

A pilot study of mianserin was conducted in a group of endogenomorphic depressive patients to test the efficacy of this tetracyclic antidepressant, to clarify the useful dose range and to determine side-effects. A maximum dose of 150mg/day was used with 10 inpatients and 15 outpatients diagnosed as suffering from RDC major depression. The dosage schedule was well tolerated, side-effects were mild, and its margin of safety was high. Continued, controlled studies of the drug are recommended. 10 references.

003242 McKnew, Donald H.; Cytryn, Leon; Buchsbaum, Monte S.; Hamovit, Joel; Lamour, Martine; Rapoport, Judith L.; Gershon, Elliot S. National Institute of Mental Health, Bldg 10, Room 3N204, 9000 Rockville Pike, Bethesda, MD 20205 **Lithium in children of lithium-responding parents.** Psychiatry Research. 4(2):171-180, 1981.

Six offspring of manic-depressive patients, whose parents were lithium responders, were selected on the basis of their incapacitating psychopathology for treatment with lithium. The children ranged in age from 6 to 12. A double-blind cross-over design was used over 16 to 18 weeks. Weekly ratings were done, and average evoked potentials (EPs) were measured at each cross-over. Two children diagnosed as having a bipolar affective disorder had a clear cut response to lithium and were strong augmenters on the EP. This, taken together with the similarity of the EP changes on lithium to those occurring in adult patients treated with lithium, supports a physiological parallel between bipolar affective illness in adults and children. 40 references. (Author abstract)

003243 Mirin, Steven M.; Schatzberg, Alan F.; Creasey, David E. Outpatient Dept., McLean Hospital, Belmont, MA 02178 **Hypomania and mania after withdrawal of tricyclic antidepressants.** American Journal of Psychiatry. 138(1):87-89, 1981.

The development of signs of hypomania or mania shortly (2 to 7 days) after drug withdrawal is reported in seven patients who had been maintained on tricyclic antidepressants. Three patients responded promptly to treatment with neuroleptics. One patient receiving lithium and three others who received no further drug treatment experienced more gradual resolution of symptoms. Tricyclic withdrawal is accompanied by changes in the turnover rate of individual neurotransmitters, as well as by shifts in the equilibrium between various transmitter systems. These events may be accompanied by alterations in mood. Although relapse to depression is more common, hypomania or mania may also occur. 12 references. (Author abstract)

003244 Musa, Mahmoud N. Research Dept., Illinois State Psychiatric Institute, 1601 West Taylor Street, Chicago, IL 60612 **Depression sub-types affect the steady-state plasma levels and therapeutic efficacy of amitriptyline and nortriptyline.** Research Communications in Psychology, Psychiatry and Behavior. 6(1):1-8, 1981.

The effect that depression has on plasma levels and the therapeutic efficacy of amitriptyline and nortriptyline were examined in 25 patients. The steady state plasma levels as well as the therapeutic response were significantly lower in patients with bipolar affective disorder than those with unipolar depression. These differences in plasma levels may be caused by differences in rates of diffusion of the drugs through membranes, capacity of drug metabolizing enzymes, rates of blood flow through the liver, or volumes of distribution. These findings lend support to the theory of biological differentiation of depression types. It is concluded that confirmation of these findings may have practical utility in pharmacotherapy of patients with affective disorders by enhancing the ability to individualize drug dosages. 15 references. (Author abstract modified)

003245 Nahunek, K.; Svestka, J.; Ceskova, E. Jihlavska 102, 657 15 Brno-Bohunice, Czechoslovakia **/Clinical experience with retard dibenzepine (Noveril 240) in endogenous depressions accompanied by symptoms of drug resistance./** Klinicke zkusenosti s retardovanou formou dibenzepinu (Noveril 240) u endogennich depresi se znamkami farmakorezistence. Ceskoslovenska Psychiatrie. 75(3):160-165, 1979.

Retard dibenzepine was administered to 42 patients (22 males and 20 females) suffering from endogenous depression, accompanied by symptoms of drug resistance. Total remission of depression was observed in 50% of the cases, and partial remission in 21%. The patients showed very good tolerance of the drug, even when they suffered from associated somatic diseases. It is concluded that patients suffering from endogenous and involutional depression do not always need to be treated with expensive drug combinations or use the convulsive method when the usual antidepressants are not effective. Treatment with retard dibenzepine is fast and effective. 13 references. (Journal abstract modified)

003246 Nutter, David; Brunswick, David. St. Joseph Hospital, 250 College Ave., Lancaster, PA 17603 **Relevancy of tricyclic antidepressant plasma levels.** American Journal of Psychiatry. 138(4):526-527, 1981.

A case report is presented of a depressed man treated with amitriptyline to illustrate some of the problems in treating depressed patients with antidepressants. The ability to measure tricyclic plasma levels in this case enabled treatment with a dose that would normally be considered ineffective. The findings have implications for studies to alleviate the toxicity of tricyclics. 7 references.

003247 O'Connell, Ralph A.; Mayo, Julia A. Dept. of Psychiatry, St. Vincent's Hospital, New York, NY **Lithium: a biopsychosocial perspective.** Comprehensive Psychiatry. 22(1):87-93, 1981.

Following a brief discussion of the impact of psychopharmacological treatment of manic-depressive illness with lithium carbonate, a review is presented of studies of patients, their families, and children to underline the importance of a biopsychosocial perspective in understanding and treating the manic-depressive patient. Data from a 10 year study are summarized including clinical response, morbidity, mortality, patient psychological and social functioning, and the impact of the disorder and lithium treatment on spouses and offspring. These studies underscore the importance of considering the multiple, complex, interacting systems of the patient, none of which alone suffice to explain etiology or to plan treatment. The patient must be understood psychodynamically as well as neurobiologically. A psychotherapeutic approach to psychosocial stressors can diminish affective episodes and enhance compliance with lithium therapy and reduce stress within the family system; family and marital therapy can reduce stress on the patient; treatment of parent and family can greatly reduce the trauma to children of growing up in a pathological household and ameliorate its developmental consequences; early casefinding and the possibility of preventive therapy for at-risk children are also facilitated. 8 references.

003248 Paykel, Eugene S. Dept. of Psychiatry, St. George's Hospital Medical School, University of London, London S.W. 17, England **Phenelzine and amitriptyline in neurotic depression. (Unpublished paper).** Final Report, NIMH Grant R05-MH-26640, 1980. 14 p.

The comparative efficacy of phenelzine, a monoamine oxidase inhbitor, and amitriptyline, a tricyclic antidepressant, was investigated in patients with depression, with particular emphasis on the clinical classifications of depression and response to treatment of subtypes. The open predictor study of 64 depressed patients showed that better response to phenelzine was found in nonhospitalized patients, less severely ill, not in Overall's retarded group, scoring at the atypical end of the Nies-Robinson Diagnostic Index, and at the anxious pole of a principal component contrasting depressive and anxiety symptoms. A double-blind controlled trial on 176 outpatients showed that both drugs produce closely similar effects in the spectrum of patients studied. 15 references.

003249 Paykel, Eugene S.; Rowan, Peter R.; Parker, Robert R. St. George's Hospital Medical School, London, England **Effects of phenelzine and amitriptyline on depression.** Psychopharmacology Bulletin. 17(1):104-106, 1981.

A double-blind study of the effects of phenelzine and amitriptyline on depression is described. Ss in the study were 131 outpatients, aged 21 to 65, with depression or mixed anxiety depression of at least 2 week duration, and rating 7 to 11 on the Raskin Three Area Depression Scale. Preliminary results suggest that both drugs are effective first line antidepressants in outpatient neurotic depressives. Effects take 6 weeks to develop fully. The two drugs appear to have substantially similar effects which are primarily antidepressant, although phenelzine also has mild antianxiety effects. Within the spectrum of patients included, which lacked severe inpatient depressives and also pure phobic disorders, the two drugs appear to effect somewhat similar groups of patients. 5 references. (Author abstract modified)

003250 Potter, William Z.; Calil, Helena M.; Extein, Irl; Muscettola, Giovanni; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Crossover study of zimelidine and desipramine in depression: evidence for amine specificity.** Psychopharmacology Bulletin. 17(1):26-29, 1981.

The effects of desmethylimipramine (DMI) and zimelidine (ZIM) on a variety of biochemical and behavioral parameters were examined in the same depressed patients. Consistent with preclinical data and pharmacokinetic findings in man, drug induced biochemical changes in the cerebrospinal fluid (CSF) showed specificity of action. DMI produced a dramatic decrease in the nonrepinephrine (NE) metabolite, 3-methoxy-4-hydroxyphenylglycol (MHPG) in CSF. ZIM had no effect on MHPG in the CSF. Conversely, ZIM reduces the serotonin (5-HT) metabolite, 5-hydroxindoleacetic acid in the CSF, while DMI did not. Results demonstrate: 1) the predicted specificity of drug action in CNS of DMI and ZIM; and 2) a dissociation of MHPG changes in CSF and urine. 12 references. (Author abstract modified)

003251 Presslich, O.; Gabriel, E.; Opgenoorth, E.; Schuster, P.; Wytek, R. Gabriel: Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1097 Wien, Austria **/Statistical analyses of physiologic data from female patients with an endomorphous depressive course: a trial, interactions between physiologic parameters, test junctures in this phase./** Statistische Analysen physiologischen Datenmaterials von Patientinnen mit endomorph-depressiven Phasenverlaufen: ein Versuch, Wechselwirkungen zwischen physiologischen Parametern, Untersuchungszeitpunkten im Verlauf der Phase und verschiedenen. Psychiatria Clinica. 13(2):65-83, 1980.

Range corrected physiological data from the parameters of heartrate (HF), respiratory rate (AF), skin potential, and skin resistance were obtained under an acoustic activation paradigm during a longitudinal study of seven women with endomorphological depression, who were treated with thymoleptic medication. Differing levels of activation were noted from six measurements: relatively low levels at the beginning and end, and high ones during the labilization phase of treatment. The varying reactivity to the diverse examination sequences of an acoustic activation program were affected little by the degree of these changes. Patient specific characteristics were as recognizable as were the stimulus specific reactions. It is concluded that each of the parameters is appropriate for estimating different physiological variables. 5 references. (Author abstract modified)

003252 Quitkin, Frederic M.; Kane, John M.; Rifkin, Arthur; Ramos-Lorenzi, Jorge R.; Saraf, Kishore; Howard, Alfreda; Klein, Donald F. New York State Psychiatric Institute, New York, NY **Lithium and imipramine in the prophylaxis of unipolar and bipolar II depression: a prospective, placebo-controlled comparison.** Psychopharmacology Bulletin. 17(1):142-144, 1981.

The relative prophylactic efficacy of lithium alone, imipramine alone, lithium plus imipramine, and placebo in both unipolar and bipolar II patients was assessed. Forty nine patients entered the study, 27 patients with unipolar illness and 22 with bipolar II illness. A significant main effect for lithium was found in preventing depressive relapse in the unipolar sample and the combined unipolar and bipolar II groups. For the bipolar II group alone, a trend is evident favoring lithium prophylaxis. No main effect of imipramine or significant lithium/imipramine interaction was evident. 7 references. (Author abstract modified)

003253 Ranelli, Candice J.; Miller, Robert E. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15261 **Behavioral predictors of amitriptyline response in depression.** American Journal of Psychiatry. 138(1):30-34, 1981.

The relationship between nonverbal behavior and treatment outcome with amitriptyline was examined in 18 female depressed patients and 18 age and sex matched control Ss. A behavioral analysis indicates that amitriptyline responders could be differentiated from nonresponders before drug treatment on the basis of discrete nonverbal behavior. Nonresponders showed a high frequency of body focused self-adaptors, posture shifts, and pauses, and a low frequency of smiles; while responders displayed long speech pauses and long durations of head aversion. 31 references. (Author abstract).

003254 Rickels, Karl; Case, W. George; Werblowsky, Joshua; Csanalosi, Irma; Schless, Arthur; Weise, Charles C. 203 Piersol Bldg., University Hospital, 3400 Spruce Street, G1, Philadelphia, PA 19104 **Amoxapine and imipramine in the treatment of depressed outpatients: a controlled study.** American Journal of Psychiatry. 138(1):20-24, 1981.

In a double blind controlled study, 158 outpatients with unipolar depression were treated for 6 weeks with amoxapine, imipramine, or placebo to assess the antidepressant effects of the new dibenzooxazepine compound, amoxapine. Of Ss, 45 amoxazepine, 43 imipramine, and 27 placebo patients completed at least 4 weeks of treatment. Active drugs produced significantly more improvement at treatment endpoint according to several physician rated measures, but patient rated measures failed to differentiate among treatments. Both active drugs, at doses up to 200mg, produced an equal amount of moderate and marked global improvement, and both produced significantly more side-effects than did placebo. 16 references. (Author abstract)

003255 Risch, Samuel C.; Cohen, Robert M.; Janowsky, David S.; Kalin, Ned H.; Sitaram, N.; Gillin, J. Christian; Murphy, Dennis L. Clinical Neuropharmacology Branch, NIMH, NIH Clinical Center, 10/3D41, Bethesda, MD 20205 **Physostigmine induction of depressive symptomatology in normal human subjects.** Psychiatry Research. 4(1):89-94, 1981.

Nine normal volunteers, screened for the absence of a personal or family history of affective disorders, and free of concurrent marihuana usage, received intravenous infusions of high dose physostigmine or saline in a randomized, double-blind counterbalanced paradigm. Self-rating and observer ratings both demonstrated a statistically significant, physostigmine associated increase in depressive type symptoms in the group as a whole, particularly pronounced in certain individuals. These results are the first report of physostigmine associated depressive symptomatology in normal subjects. While the ratings are discrepant with two previous studies, the use of multiple self-ratings and some differences in physostigmine dosage and infusion times might have contributed to this difference. These findings suggest that high dose physostigmine may represent a pharmacological model of depression in normal subjects, or alternatively may be diagnostic of vulnerability to affective disorder in certain subjects free of a previous history of affective disturbances. 13 references. (Author abstract)

003256 Rounsaville, Bruce J.; Klerman, Gerald L.; Weissman, Myrna M. Substance Abuse Treatment Unit, Connecticut Mental Health Center, 100 Park St., New Haven, CT 96511 **Do psychotherapy and pharmacotherapy for depression conflict? Empirical evidence from a clinical trial.** Archives of General Psychiatry. 38(1):24-29, 1981.

Six hypotheses about negative interactions between pharmacotherapy and psychotherapy are evaluated on the basis of data derived from a clinical trial of psychotherapy and tricyclic antidepressants alone and in combination as treatment for ambulatory depression. These hypotheses are: 1) the negative placebo effect; 2) drug induced reduction of symptoms reduces motive for continuing psychotherapy; 3) pharmacotherapy undercuts defenses; 4) deleterious effects of pharmacotherapy on psychotherapy expectations; 5) psychotherapy may be symptomatically disruptive; and 6) biochemical replacement effect of drugs. None of the hypotheses was supported by the data. As has been shown in other reports the combination of treatments was more effective than either treatment alone. 17 references. (Author abstract modified)

003257 Rush, A. John; Watkins, John T. Dept. of Psychiatry, Southwestern Medical School, 5323 Harry Hines Blvd., Dallas, TX 75235 **Group versus individual cognitive therapy: a pilot study.** Cognitive Therapy and Research. 5(1):95-103, 1981.

Outcome in group versus individual cognitive therapy was assessed, along with the effects of antidepressant medication on attendance and outcome in 44 depressed Ss. Contrary to expectations, the efficacy of group therapy was not as great as individual treatment (with or without medication), as measured by the Beck Depression Inventory. The Hamilton Rating Scale for Depression (HRS-D) on a subsample did not, however, result in between groups differences at posttreatment. The addition of medication to individual therapy did not significantly reduce end of treatment symptom levels in this small sample. The symptom response pattern during active treatment suggests that group therapy initially produces as rapid symptom reduction as do other treatments, but a less complete response is evident at the end of treatment. 22 references.

003258 Sebastiani, G. Cattedra di Clinica Psichiatrica II, Universita di Bari, Bari, Italy **/Lithium uptake in red cells of cycloid and unipolar dysthymic patients./** Captazione del litio nei globuli rossi di pazienti con psicosi cicloide e distimia unipolare. Rivista Sperimentale di Freniatria. 103(2):375-379, 1979.

Lithium uptake in red cells was studied in 32 patients with affective disorders, psychosis, and depression. The sample consisted of 18 men and 14 women, between ages 40 and 70, who had not received previous lithium therapy. A control group also was established with 19 healthy volunteers. The lithium red blood cell and plasma ratio was estimated in vitro at different times throughout the experiment. Since no significant differences in lithium ratio were found between controls and either of the diagnostic groups, it is concluded that no differences in the rate of uptake of lithium into red blood cells exist between controls and cycloid psychotics or unipolar depressives. 13 references. (Journal abstract modified)

003259 Sharma, Shridhar; Hegde, Rajendra. Dept. of Psychiatry and Human Behaviour, Goa Medical College, Panaji, Goa, 403 001, India **Therapeutic efficacy of doxepin in divided and single dose regime.** Indian Journal of Psychiatry. 22(3):283-287, 1980.

The effect of doxepin hydrochloride on depression was examined in 38 patients suffering from depression as a primary illness. Patients were randomly allocated to either a three times daily dosage group or a single nocturnal dose group with no attempt to make the sexes equal in the sampling. In 11 patients symptoms were cleared, 22 showed marked improvement, 4 showed moderate improvement, 1 showed slight improvement, and in 1 there was no improvement. Divided and single dosage regimens did not cause any differences in therapeutic effectiveness nor was there a significant difference in the incidence of side-effects. It is concluded that the single nocturnal dosage of doxepin is well tolerated and is as effective as the thrice daily dosage schedule. 14 references.

003260 Siomoupoulos, V. Inpatient Psychiatric Unit, Ravenswood Hospital Medical Center, 1931 W. Wilson, Chicago, IL 60640 **Is mania overdiagnosed?: the three common pitfalls in diagnosing manic-depressive illness.** Behavioral Medicine. 8(3):21-23, 1981.

Three common pitfalls in the misdiagnosis of manic-depressive illness and/or inappropriate lithium treatment are discussed. Popular media publicizing of lithium as a miracle drug for eliminating manic-depressive mood swings has contributed to requests for lithium therapy by patients with ups and downs associated with hysterical personality. Because grandiosity, hyperactivity, and pressured speech are symptoms common to both the manic and the excited paranoid schizophrenic patient, it is not uncommon to find this type of paranoid schizophrenic receiving lithium therapy because of misdiagnosis. The therapeutically overzealous psychiatrist may prescribe lithium for the functioning hypomanic patient whose episodes characteristically are rare, mild, and tend to dissipate without treatment. The features of hysterical personality, paranoid schizophrenia, and mild hypomania, coupled with a positive placebo effect can mislead the psychiatrist into prescribing unwarranted lithium treatment. Lithium side-effects are presented in tabular form. 4 references.

003261 Soucek, K.; Zvolsky, P. Ke Karlovu 11, 128 02 Praha 2, Czechoslovakia **/Lithium in 1978./** Lithium v roce 1978. Ceskoslovenska Psychiatrie. 75(5):363-368, 1979.

Basic research and clinical research in 1978 concerning lithium salts are surveyed. The knowledge about the transportation system of lithium has expanded, but the research has also become very complicated. Fieve and associates studied the kinetics of the efflux of lithium from erythrocytes and found that there is no connection between the plasma level, the doses of lithium, and the result of prophylaxis. It is concluded that lithium is not effective in the treatment of schizophrenia, acute exacerbations of schizoaffective psychoses, acute depression, anxiety, abuse of opiates, periodic hyperkalemic paralysis, and the hyperkinetic syndrome. 26 references.

003262 Stewart, Jonathan W.; Quitkin, Frederic; Liebowitz, Michael R.; McGrath, Patrick J.; Klein, Donald F. New York State Psychiatric Institute, New York, NY **Efficacy of desipramine in mildly depressed patients: a double-blind, placebo-controlled trial.** Psychopharmacology Bulletin. 17(1):136-138, 1981.

A double-blind, placebo controlled trial of the efficacy of desipramine in mildly depressed patients is described. The desipramine and placebo response rates in these mildly depressed patients approach tricyclic antidepressant (TCA) and placebo response rates usually quoted for moderately to severely depressed patients. Thus, severity of illness may not be a useful criterion for predicting the utility of TCA. Since persistence of dysphoric mood is required for a diagnosis of major depressive disorder and precludes a diagnosis of intermittent depressive disorder, these data suggest that persistence of dysphoric mood may be a more useful indication for TCA use than severity of illness. 11 references.

003263 Straumanis, John J., Jr.; Shagass, Charles; Roemer, Richard A.; Mendels, Joseph; Ramsey, T. Alan. Temple University Medical Center, Philadelphia, PA **Cerebral evoked potential changes produced by treatment with lithium carbonate.** Biological Psychiatry. 16(2):113-129, 1981.

The evoked potential (EP) changes of 12 depressive patients were studied while they were on placebo and on therapeutic doses of lithium carbonate (Li). Li produced a number of amplitude changes in EPs of all sensory modalities, while there were few latency changes; in general, amplitudes of positive components were increased, while negative component amplitudes were reduced. Spatial distributions of EP peaks were mainly unaltered. The amount of EP amplitude change with Li tended to be correlated with plasma and erythrocyte Li levels. No convincing correlations were found between alterations in EPs and depression ratings. The findings indicate that Li produces more widespread CNS changes than suggested by previous reports; it appears that these tend to be related to Li levels, but not to the therapeutic effects of Li. 32 references. (Author abstract modified)

003264 Svestka, J.; Nahunek, K.; Ceskova, E.; Rysanek, R. Psychiatricka Klinika FNsP, Jihlavska 102, 657 15 Brno-Bohunice, Czechoslovakia **/Therapeutic effect of mianserine and imipramine in endogenous depressions (controlled comparison)./** Lecebny ucinek mianserinu a imipraminu u endogennich depresi (kontrolovane srovnani). Ceskoslovenska Psychiatrie. 75(5):316-323, 1979.

Two antidepressants, mianserine and imipramine, were used in a double-blind study of 82 cases of hospitalized patients suffering from endogenous depression. The subjects treated with mianserine showed a significantly smaller number of complete remissions and discharges from hospital. In those cases where it was possible to make individual comparisons, the treatment with imipramine produced better results in nine cases, the same results in six cases. The validity of the finding was affected by the fact that most of the patients compared individually were treated with imipramine after they had been treated unsuccessfully with mianserine. Side-effects of the anticholinergic type were significantly less frequent when mianserine was used. 8 references. (Author abstract modified)

003265 Symonds, Richard L.; Williams, Paul. Williams: Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **Lithium and the changing incidence of mania.** Psychological Medicine. 11(1):193-196, 1981.

The effect of lithium containing compounds on admission rates of mania patients in England was studied to hospitals using hospital admission data for 1970 to 1975. For males but not for females, there was a decrease in the proportion of all new admissions given a diagnosis of mania between 1970 to 1971. However, from 1971 to 1975, years which saw large increases in lithium prescription, mania admissions increased (relative to all admissions). A similar picture was exhibited by male readmissions: the proportion of all readmissions given a diagnosis of mania decreased from 1970 to 1972, and increased thereafter. For female readmissions, however, there was a trend of increase in mania admissions, both absolute and relative, across the time period. Possible explanations for the findings are proposed. 6 references. (Author abstract modified)

003266 Tanimoto, Kenji; Maeda, Kiyoshi; Yamaguchi, Naohiko; Chihara, Kazuo; Fujita, Takuo. Dept. of Psychiatry, Kobe University School of Medicine, 7 Kusunoki-cho Ikuta-ku, Kobe

650, Japan **Effect of lithium on prolactin responses to thyrotropin releasing hormone in patients with manic state.** Psychopharmacology. 72(2):129-133, 1981.

Plasma thyrotropin (TSH) and prolactin (PRL) responses to thyrotropin releasing hormone (TRH) were studied before and during lithium treatment for 3 to 4 weeks in six patients with manic states and eight control Ss. Lithium administration did not alter nonstimulated secretion of TSH in any groups, but resulted in exaggerated responses of plasma TSH to TRH in both groups. No difference between the two groups was observed before lithium treatment or in plasma TSH responses to TRH during lithium treatment. The observed augmented responses of plasma PRL to TRH in patients with manic states suggest the existence of some abnormality in the hypothalamo/pituitary axis. Results are discussed in relation to the hypothesized mechanisms by which lithium affects manic symptoms. 27 references. (Author abstract modified)

003267 Vacek, J. Poliklinika OUNZ, 360 66 Karlovy Vary, Czechoslovakia **/Confession of a melancholiac: contribution to the problem of prophylaxis of manic-depressive psychosis using lithium./** Zpoved melancholika: prispevek k problemu profylaxe maniodepresivni psychozy soli lithia. Prakticky Lekar. 59(19-20):738-740, 1979.

A patient suffering from manic-depressive psychosis was treated with daily doses of lithium salts over a 3 year period. His mental state eventually was stabilized. The patient gave a detailed description of his experience during the treatment and during the process of recovery in personal letters, parts of which are presented. These letters illustrate the deep changes taking place in the patient's mind during these 3 years, and they provide valuable information about the subjective feelings and observations of a patient suffering from endogenous depression.

003268 Van Houtte, J. P.; Horwitz, Monique; Becu, Roland; Delarue, Michel; Domengie, Bernard; Lupczynski, Georges. Hospitalo-Universitaire de Sante Mentale et de Therapeutique, 100-102, rue de la Sante, F-75673 Paris Cedex 14, France **/The treatment of depression using clomipramine in general medical practice: 48 cases treated on an outpatient basis./** Traitement des etats depressifs par la clomipramine dans la pratique de medecine generale: a propos de 48 observations traitees en cure ambulatoire. Psychologie Medicale. 12(7):1561-1576, 1980.

The treatment of outpatient cases of depression with clomipramine was studied. The drug was administered to 48 patients suffering from depression. Dosages averaged between 75mg and 100mg daily; the duration varied depending on results, tolerance, and the need to prolong treatment. Results show that reactive depressions responded the best, with 90% reporting good or very good results. Clinical tolerance was good; side-effects were modified or reduced. 218 references. (Journal abstract modified)

003269 van Praag, Herman M. Psychiatric University Clinic, University of Utrecht, Utrecht, The Netherlands **Management of depression with serotonin precursors.** Biological Psychiatry. 16(3):291-310, 1981.

An overview is presented of management of depression with 5-hydroxytryptamine (5-HT, serotonin) precursors. The 5-HT hypothesis of pathogenesis in depression is examined within the context of the background of 5-HT treatment. The justification of the 5-HT precursor strategy, which aims to increase the availability of 5-HT in the brain, is outlined; and a summary of early studies of the effects of 5-hydroxytryptophan (5-HTP) treatment in depressed and normal Ss are summarized. Although the number of studies comparing 5-HTP with placebo or standard antidepressants is still small, results indicate that 5-HTP has antidepressant properties and that the 5-HTP/clomipramine combination is superior in effect than either compound alone. Results of tryptophan studies have been less unequivocal than those of 5-HTP studies, tryptophan being found effective in only five of ten double-blind comparative studies, possibly as a result of pharmacokinetic factors. 91 references.

003270 Versiani, Marcio. Av. N S. de Copacabana, 1133, conj. 1303, 22070, Rio de Janeiro, Brazil **/Therapeutics (I) -- pharmacological treatment of depressions./** Terapeutica (I) – o tratamento farmacologico das depressoes. Jornal Brasileiro de Psiquiatria. 28(1-4):17-22, 1979.

The therapeutic management of depressive states is examined. The mechanism of action of antidepressants seems to be related to the neurotransmitters. Antidepressants favorably affect psychotic depression. In other depressions antidepressants are not effective and may even aggravate symptoms. Tricyclic antidepressants remain in the body up to 3 days, are potent anticholinergic agents, and should be prescribed in dosages beween 75 and 250mg/day. Dosages should be smaller in children and the elderly, since their less effective metabolism can cause lethal intoxication. Monoamine oxidase inhibitors have been used by some researchers to treat neurotic depression, but there is still no real scientific basis for this therapy. 28 references. (Journal abstract modified)

003271 Watanabe, Shosuke; Yokoyama, Shigeo; Kubo, Shinsuke; Iwai, Hiroyuki; Kuyama, Chie. Dept. of Psychiatry, Kawasaki Medical School, Kurashiki, Japan **Relationship between blood concentrations and clinical effects of a new antidepressant** Folia Psychiatrica et Neurologica Japonica. 34(2):147-156, 1980.

In the course of a double-blind controlled study of antidepressants, observations were carried out on the relationship between maprotiline/desmethylmaprotiline concentrations in blood and antidepressive effects, the doses, and the incidence of side-effects. The maprotiline concentration in the effective group (markedly improved and moderately improved) was 306.9 plus or minus 112.9ng/ml and 244.4 plus or minus 43ng/ml in the non-effective group (slightly improved, unchanged, or aggravated). There was no statistically significant difference between the groups. Correlations of the maprotiline concentrations in blood, and together with desmethylmaprotiline concentrations, with variation rates in Hamilton depression scores show a tendency toward higher concentrations in blood with higher therapeutic responses. Side-effects were observed in all patients with blood concentrations higher than the mean value (265.2ng/ml). 14 references. (Author abstract)

003272 Weissman, Myrna M.; Klerman, Gerald L.; Prusoff, Brigitte A.; Sholomskas, Diane; Padian, Nancy. Yale University School of Medicine, Suite 2A, 904 Howard St., New Haven, CT 06519 **Depressed outpatients: results one year after treatment with drugs and/or interpersonal psychotherapy.** Archives of General Psychiatry. 38(1):51-55, 1981.

A 1 year followup was conducted on ambulatory nonbipolar, nonpsychotic, acutely depressed patients who received amitriptyline hydrochloride and/or interpersonal psychotherapy (IPT), each alone and in combination, as part of a 4 month clinical trial. There were no differential long-term effects of the initially randomized treatment on clinical symptoms 1 year later, since most of the patients were asymptomatic. While most patients were functioning reasonably well, there were some main effects of IPT on social functioning at the 1 year followup. Patients who received IPT with or without pharmacotherapy were doing significantly better on some measures of social functioning. 20 references. (Author abstract)

003273 White, Kerrin. University of Southern California School of Medicine, Dept. of Psychiatry and the Behavioral Sciences, Los Angeles, CA **The benefits and risks of combining an MAO inhibitor and a tricyclic antidepressant.** Psychopharmacology Bulletin. 17(1):106-107, 1981.

A pilot study concerning the benefits and risks of combining a monoamine oxidase (MAO) inhibitor (tranylcypromine) and a tricyclic antidepressant (amitriptyline) is described. Thirty depressed inpatients were randomly assigned to treatment with either drug alone or in combination (at half dosages of each). No significant differences in therapeutic efficacy or frequency of side-effects were found among the treatment groups. These findings seem consistent with the body of literature on the combination, which has appeared relatively safe when used in a recommended manner, but without any convincing evidence for therapeutic advantage. 8 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

003274 Ban, Thomas A. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Psychopharmacology of neuroses.** Psychosomatics. 22(1):55, 58-60, 1981.

A number of neurotic disorders are reviewed with regard to the effectiveness of various classes of psychopharmacologic agents and the current understanding of the pharmacologic basis for their therapeutic effects. These disorders include generalized anxiety disorders, panic disorders, obsessive-compulsive disorders, the phobic anxiety depersonalization syndrome, depressive neurosis, and psychophysiologic disorders. Drugs used in these disorders include sedatives, tricyclic antidepressants, and monoamine oxidase inhibitors. 19 references. (Author abstract modified)

003275 Bunney, William E., Jr. Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **/Recent advances in the diagnosis and treatment of anxiety disorders./** Introduction. Psychiatric Annals. 11(1):7, 1981.

Recent advances in the diagnoses and treatment of severe anxiety disorders are noted. Useful diagnostic categories in the areas of anxiety disorders have been defined in the new edition (third) of the Diagnostic and Statistical Manual of Mental Disorders; these categories have become increasingly meaningful because of the differential and increasingly successful response of some of these disorders to pharmacological agents such as monoamine oxidase inhibitors, tricyclic compounds, benzodiazepines, and propranolol. The discovery of benzodiazepine receptors in human brain may contribute to greater understanding of the action of these compounds and may eventually lead to the identification of a naturally occurring anxiety or antianxiety compound produced within the brain that may play an important role in mediating behavioral symptoms of anxiety.

003276 Bunney, William E., Jr. Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Current biologic strategies for anxiety.** Psychiatric Annals. 11(1):21,24-25,28-29, 1981.

A review of recent biological research into the mode of action of pharmacologic agents that effect human anxiety is presented. Areas reviewed inlclude: the recent discovery of receptors in the human brain for the most effective of the anxiolytic compounds, benzodiazepines; information concerning the action of benzodiazepines, specifically the role of GABA; the criteria for an endogenous benzodiazepine and some proposed endogenous compounds; and the possible role of the locus coruleus in anxiety. Some earlier data concerning the role of sodium lactate in producing anxiety like symptoms are also summarized. Advances on several fronts provide reason to hope that new understanding of the causes, prevention, and treatment of anxiety will soon be forthcoming. 37 references.

003277 Cohen, Neal L.; Alpert, Murray; Friedhoff, Arnold J. New York University Medical Center, New York, NY 10016 **Clinical trial of halazepam and clorazepate: considerations of a single bedtime dose.** Psychopharmacology Bulletin. 17(1):134-135, 1981.

The efficacy of halazepam in a single bedtime dose was compared with clorazepate and placebo in the treatment of patients with symptoms of anxiety and tension, whether or not accompanied by somatization and/or mild depression. At the end of the first week of treatment, significant differences favoring both drug groups over placebo were found on physician rated measures of efficacy, including global assessments, relative improvement, and Hamilton Anxiety Scales. These significant differences favoring either drug over placebo persisted throughout the 4 week study. Patient rated global assessments, however, did not discriminate well between drug and placebo groups. Advantages of one a day bedtime dosaging are discussed. 1 reference.

003278 Frank, Linda Ann. Fielding Institute **Comparison of anxiety reducing substances. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3176-B, 1981. Ann Arbor, Univ. Microfilms No. 8103055, 68p., 1980.

Diazepam, Valerian, and placebo were compared with respect to the reduction of anxiety. A daily global scale showed that subjects felt significantly better while taking diazepam than while taking placebo. There was no significant difference between the effects of diazepam and Valerian or between Valerian and placebo. Valerian was found to be significantly different from diazepam and placebo with respect to anxiety reduction, and the effets of Valerian on general well-being did not differ significantly from those of placebo. It is suggested that the process of obtaining more information regarding the existence and effect of psychoactive properties in Valerian would require studies in which the subjects take larger doses of Valerian for a longer period of time. (Journal abstract modified)

003279 Hervy, C. C.H.U., Limoges, France **/Clinical trials with clobazam in geriatrics./** Essais cliniques du clobazam en geriatrie. Revue de Geriatrie. 5(4):201-203, 1980.

The use of clobazam in the treatment of anxiety in the elderly was investigated. Clobazam was administered to 30 Ss (25 women and 5 men) over age 67, in doses of 10mg for 1 to 3 months, depending on the S. Results show that 75% of the Ss benefitted from this therapy with an important lasting improvement. Tolerance was good, but vigilance disturbances and secondary effects were common among the elderly during drug treatment; therefore, precautions are essential.

003280 Kessler, Kenneth A. Section on Psychopharmacology, Psychiatric Institute, Washington, DC **Drug treatment of the phobic-anxiety syndrome.** Psychiatric Annals. 11(1):41,45-48, 1981.

Drug treatment of phobic anxiety syndrome is examined in a review of the relevant research literature. One of the earliest reported uses of drug treatment for phobic anxiety was Dally's (1958) treatment of patients with mild depressive states with anxiety features using the monoamine oxidase inhibitor (MAOI), iproniazid. In a 1962 study, Sargent and Dally reported marked improvement in 74% of a sample of 245 phobics treated with an MAOI, and Klein (1962) found equally favorable results with tricyclics. The results of these seminal studies have subsequently been confirmed by others, and both MAOIs and tricyclics are now generally accepted as being effective treatments for phobic anxiety disorders. Beta blockers, such as propranolol, may also play a limited role in the management of phobias, specifically, in alleviating the physical symptoms that accompany anxiety attacks. There is now a substantial body of literature reporting 40% to 50% complete remission of phobic anxiety syndrome treated with MAOIs; phenelzine is generally the drug of choice. Tricyclics, particularly chlorpromazine, have been found equally effective. Clinical outcome is improved when either of these drugs are supplemented by behavior therapy to overcome the phobic avoidance and benzodiazepines to minimize anticipatory anxiety. 31 references. (Author abstract modified)

003281 Leme-Lopes, J. Rua Dona Mariana, 53, ap. 1.401, Rio de Janeiro, Brazil **/Changes in the psychopathology of psychosis due to neuroleptic treatment./** Mudanca da psicopatologia das psicoses sob a acao dos neurolepticos. Jornal Brasileiro de Psiquiatria. 28(1-4):1-6, 1979.

The role of neuroleptics in the transformation of the psychopathology of schizophrenic psychosis is discussed. The effects of neuroleptics can be summarized in five categories: sedative, sleep/awake continuum, antimaniacal, antipsychotic, and neurologic. Neuroleptics are effective therapeutic agents for delusions and hallucinations. Autism and emotional insensibility are not influenced by the same doses and therapeutic schedules used for delusional and hallucinatory states. It is concluded that the change in the psychopathology of psychosis can be observed best in neuroleptic treatment. 26 references. (Journal abstract modified)

003282 McNair, Douglas M. Boston University, School of Medicine, Boston, MA 02118 **Methodology of outpatient drug research. (Unpublished paper).** Final Report, NIMH Grant R01-MH-27452, 1980. 11 p.

Data from three clinical trials -- symptomatic volunteers (SVs) from a general population, SVs from a student population, and college student psychiatric patients -- were examined to determine: 1) pharmacotherapy of anxiety and depression in SVs; 2) pharmacotherapy of phobic anxiety in SVs; and 3) pharmacotherapy of anxiety in student patients and student SVs. Benzodiazepine, imipramine, and placebo are compared for anxiety and depression; and chlordiazepoxide and imipramine are compared for agoraphobia. The data show that anxiety, placebo plus psychotherapy was clearly and significantly superior to the administration of chlordiazepoxide plus psychotherapy across many criteria. 19 references.

003283 Rees, Linford; (Saiz-Ruiz, J.; Valbuena, A., translators). St. Bartholomew's Hospital, London, England **/Treatment of anxiety states./** Tratamiento de los estados de ansiedad. Actas Luso-Espanolas de Neurologia, Psiquiatria etc. 8(2):5-10, 1980.

The treatment of anxiety syndromes is discussed. Three forms of treatment have proved useful: pharmacotherapy, biofeedback, and behavioral therapy. The most prominent treatment is pharmacotherapy, using the following drugs: barbiturates, carbamates, clormezanone, clormetiazol, beta-blockers, neuroleptics, tricyclic antidepressants, monoamine oxidase inhibitors, and benzodiazepines. The differences between various benzodiazepines are discussed in detail. It is concluded that the use of drugs is an important method in the treatment of anxiety conditions. 4 references.

003284 Shader, Richard I.; Greenblatt, David J.; Ciraulo, Dominic A. Dept. of Psychiatry, Tufts University School of Medicine, Boston, MA **Benzodiazepine treatment of specific anxiety states.** Psychiatric Annals. 11(1):30, 37-40, 1981.

A classification system of anxiety states is presented to provide a rational basis for pharmacological treatment. Although there is considerable overlap and anxiety patterns may coexist, anxiety states may be divided into eight subtypes: 1) situational anxiety which is often helped by treatment with a short acting benzodiazepine, such as lorazepam or oxazepam, in conjunction with psychotherapy or behavior modification; 2) free floating anxiety, longer acting benzodiazepines (diazepam, chlordiazepoxide, clorazepate, prazepam) may be indicated, although insight oriented psychotherapy may be needed for definite relief; 3) and 4) phobic and anticipatory anxiety, benzodiazepines may be helpful in anticipatory anxiety, but imipramine or phenelzine may also be needed to treat phobic anxiety, possibly in conjunction with desensitization; 5) anxiety with depression, which is often best treated with a sedating antidepressant such as amitriptyline or doxepin, although masked or atypical depressions may respond best to a monoamine oxidase inhibitor; 6) traumatic anxiety, such as may be seen as part of stress disorders, and which may require a total treatment approach including short-term prescription of benzodiazepines; 7) anxiety secondary to medication and medical conditions; and 8) psychotic terror.

003285 Solyom, C.; Solyom, L.; LaPierre, Y.; Pecknold, J.; Morton, L. Shaughnessy Hospital, Vancouver, British Columbia, Canada **Phenelzine and exposure in the treatment of phobias.** Biological Psychiatry. 16(3):239-247, 1981.

A double-blind study was carried out on 40 agoraphobic and socially phobic patients, matched and then randomly assigned to one of four treatment groups: phenelzine-exposure, phenelzine-no exposue, placebo-exposure, placebo-no exposure. Exposure consisted of encouraging the patient to face the phobic situation a predetermined number of times. Assessments made at the beginning and end of 8 weeks of therapy and 8 weeks thereafter, show that the phobia ratings of groups decreased significantly. The combined exposure group improved significantly more than the combined no exposure group during treatment. At 8 week followup, there was some deterioration in the phenelzine-exposure and palcebo-no exposure groups. Exposure, with or without phenelzine, was the superior treatment modality. The antiphobic effect of phenelzine was not supported, although it seemed to reduce subjective anxiety during exposure experiences. The possibility that effect of phenelzine is dose related is discussed. 16 references. (Author abstract)

003286 Stahl, Stephen M.; Berger, Philip A. Stanford Mental Health Clinical Research Center, Dept. of Psychiatry and Behavioral Sciences, School of Medicine, Stanford, CA 94305 **Physostigmine in Tourette syndrome: evidence for cholinergic underactivity.** American Journal of Psychiatry. 138(2):240-242, 1981.

Improvement in Tourette syndrome symptoms following physostigmine administration in a double-blind, placebo controlled investigation with six male patients is reported. The findings support the hypothesis that Tourette syndrome is characterized not only by a relative excess of central dopaminergic activity, but also by a relative deficiency in central cholinergic activity. This is consistent with the concept that the pathophysiology of hyperkinetic movement disorders is based on an imbalance in central dopamine-acetylcholine neuronal activities. Implications for the clinical treatment of Tourette syndrome are discussed, especially as related to use of the neuroleptic, haloperidol, which has unacceptable side-eefects in dosages that control tics and can produce permanent tardive dyskinesia. 10 references.

003287 van der Velde, Christiaan D. Abraham Ribicoff Research Center, P.O. Box 508, Norwich, CT **Maprotiline versus imipramine and placebo in neurotic depression.** Journal of Clinical Psychiatry. 42(4):138-141, 1981.

The antidepressant effect of maprotiline, a tetracyclic compound, was compared with that of imipramine in a 4 week, double-blind, placebo controlled study with neurotic depressives. On all factors of the Hamilton Depression Rating Scale and on most items of the Zung Self-Rating Scales for Depression and Anxiety, maprotiline appeared slightly more effective than did imipramine and showed a faster onset of action. In addition maprotiline appeared to cause fewer anticholinergic side-effects. 10 references. (Author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

003288 Asam, Uta; Karrasz, W. Abt. fur Kinder- und Jugendpsychiatrie, Universitat Hamburg, Martinistrasse 52, D-2000 Hamburg 20, West Germany **/Child psychiatry and psychopharmacotherapy in general practice, in pediatrics, and in neurology./** Allgemein-, kinder- und nervenarztlichen Praxis. Zeitschrift fur Kinder- und Jugendpsychiatrie. 7(3):221-231, 1979.

A questionnaire was used to obtain information from 270 general practitioners, pediatricians, and neurologists in Hamburg about their child psychiatric work. Analysis of the responses shows that pediatricians in particular treat many children with psychiatric problems. A third of these children are given psychotropic drugs. A comparable study planned for all of West Germany did not materialize. 6 references. (Journal abstract modified)

003289 Avanesova, T. S.; Sviridova, Ye. I. Tsentral'nyy NII sudebnoy psikhiatrii imeni prof. Serbskogo, Moskva, USSR / **The therapeutic activity of tryptophan and its effect on serotonin metabolism in epileptic patients./** Terapevticheskaya aktivnost' triptofana i yego vliyaniye na obmen serotonina u bol'nykh epilepsiyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(6):857-863, 1980.

The therapeutic effects of tryptophan were studied in a group of 24 epileptic patients of various ages and durations of illness. The patients were given dosages of .25g of tryptophan three times daily. As a result, a decreased initial level of serotonin was noted in the patients, particularly in those with frequent epileptic seizures and with a long history of the disorder. After as little as a week of its administration, the tryptophan began to produce a reliable increase in the serotonin level as well as positive changes in the clinical picture. These effects were especially notable in patients with grand-mal seizures and with personality disorders. 14 references. (Journal abstract modified)

003290 Baratz, Robin; Mesulam, Marek-Marsel. Behavioral Neurology Unit, Beth Israel Hospital, 330 Brookline Avenue, Boston, MA 02215 **Adult-onset stuttering treated with anticonvulsants.** Archives of Neurology. 38(2):132, 1981.

A case report is presented in which stuttering and aphasia emerged as salient clinical features in an adult with multifocal brain damage and paroxysmal EEG activity. In addition, this patient had a bilaterally abnormal EEG with notable paroxysmal discharges in the left temporal region. Anticonvulsant treatment was associated with reversal of the stuttering and with marked improvement in language abilities. Even though the patient had structure, the abnormality in the EEG still appeared to have significant implications in terms of therapy since the stuttering responded to anticonvulsant medications. 8 references. (Author abstract modified)

003291 Barthelemy, C.; Garreau, B.; Leddet, I.; Sauvage, D.; Domenech, J.; Muh, J. P.; Lelord, G. Service d'Explorations Fonctionnelles Psychopathologiques, C.H.U. Bretonneau, F-37044 Tours Cedex, France **/The biological and clinical effects of oral magnesium and associated magnesium-vitamin B6 administration on certain disorders observed in infantile autism./** Effets cliniques et biologiques de l'administration orale du magnesium seul ou du magnesium associe a la vitamine B6 sur certains troubles observes dans l'autisme infantile. Therapie. 35(5):627-632, 1980.

Two sequentially crossed double-blind therapeutic trials were performed using 37 severely autistic children 4 to 15 years old. In Experiment 1 with 21 children, magnesium/vitamin B6 (B6-Mg) was tested against placebo. In Experiment 2 with 16 children B6-Mg was tested against magnesium Mg alone. The therapeutic effects observed were evaluated using quantitative clinical scales. Urinary titers of homovanillic acid (H.V.A.) were assayed before, during, and after treatment and compared with urinary H.V.A. levels of normal children of the same age who acted as controls. The clinical results confirmed a moderate therapeutic action of the B6-Mg association. The effects of Mg administered alone were comparable to those obtained with associated B6-MG. Urinary H.V.A. levels were initially higher in the autistic children than in the control group of children. Treatment with the B6-Mg association decreased urinary H.V.A. in the autistic group. An identical effect was observed in the children treated with Mg alone. 22 references. (Journal abstract)

003292 Bernstein, Jerold G. Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **/Reflections on antipsychotic chemotherapy: the beginning of pharmacological treatment./** Reflexiones sobre la quimioterapia antipsicotica: el comienzo del tratamiento farmacologico. Acta Psiquiatrica y Psicologica de America Latina. 26(3):248-255, 1980.

An interview concerning the use of antipsychotic drug treatment of schizophrenic, manic-depressive, psychotic depressive, and chronically anxious patients is presented. The psychiatrist must find out as much as possible about the patient's possible reaction to the drug and any family antecedents involving the use of the drug. Symptoms, age, behavior, medical complications, and possible side-effects must be considered. Often, the best drug is found through a process of trial and error. Dosage may vary radically from patient to patient. Most patients cooperate best when they are told to take only one dosage daily. The use of drugs has made the treatment of the psychotic within the community more common than lengthy periods of hospitalization.

003293 Bobon, D. P.; Detaille, J.; Leunen, A.; Born-Leveque, M. Clinique psychiatrique universitaire, Rue Saint-Laurent 58, B-4000 Liege, Belgium **/Alcohol withdrawal using tiapride: quantitative psychopathology./** Le sevrage ethylique par tiapride: psychopathologie quantitative. Acta Psychiatrica Belgica. 80(2):156-162, 1980.

The alcoholic's psychological status during treatment with tiapride was studied. Nineteen hospitalized male alcoholics were administered 400mg three times daily of tiapride during the first 4 days of alcohol withdrawal and 300mg orally during the following 10 days. The majority of the alcoholics demonstrated improvement in withdrawal related disturbances. Results confirm the rapidity of tiapride's action as well as its efficiency and harmlessness at the prescribed dosage. The drug was better tolerated than the usual neuroleptics and involved smaller potential risks of substitutive drug addiction than the anxiolytic drugs or paraldehyde. 6 references. (Journal abstract modified)

003294 Bobruff, Arthur; Gardos, George; Tarsy, Daniel; Rapkin, Robert M.; Cole, Jonathan O.; Moore, Patricia. 70 Crestwood Rd., West Newton, MA 02165 **Clonazepam and phenobarbital in tardive dyskinesia.** American Journal of Psychiatry. 138(2):189-193, 1981.

A controlled study investigated clonazepam versus the active placebo of phenobarbital in 21 psychiatric patients with tardive dyskinesia to determine advantages of benzodiazepines over other antidyskinetic drugs. Both drugs significantly reduced dyskinetic movements. Clonazepam had a stronger effect on orofacial dyskinesia, and phenobarbital was more effective for limbs and axial movements. Clonazepam was also more effective for drug free Ss and those receiving low doses of neuroleptics than for all patients given phenobarbital and for clonazepam patients taking high doses of neuroleptics. It is suggested that future treatment studies focus on the effects of antidyskinetic drugs on distinct body regions. 19 references. (Author abstract modified)

003295 Bocci, U.; Beretta, G. Ospedale Psichiatrico, Castiglione delle Stiviere (Mantova) Italy **/Hypnotic action of flunitrazepam (Roche's Roipnol) in patients with severe psychiatric disorders./** Azione ipnotica del flunitrazepam (Roipnol Roche) in soggetti con gravi turbe psichiatriche. Rivista Sperimentale in Freniatria. 103(1):201-211, 1979.

The hypnotic action of flunitrazepam on patients with severe psychiatric disturbances was studied. The first group of subjects included 24 men and women suffering from severe insomnia with a high degree of anxiety. The second group included 16 male subjects; 11 were drug addicts with withdrawal syndrome, and the other 5 suffered from manic episodes. Both groups were administered between 2 and 8mg of the drug. At the beginning of the study and during the subsequent 7 days of therapy, the following measures were recorded and rated: sleep latency, sleep duration, sleep quality, nighttime awakenings, and the condition the following morning. The drug was most effective with regard to sleep latency, sleep duration, and number of nighttime awakenings, with improvement ranging from 71.27% to 82.93%. After 7 days of treatment the total improvement was 82.54% in the first group and 75.13% in the second group. It is conclude that flunitrazepam is superior to other commonly used hypnotics and does not intefere with clinical tests and blood pressure. 14 references. (Journal abstract modified)

003296 Bonnaffoux, Daniel; JeanParis, Francois. Hopital de Saint-Remy-Clairefontaine, F-70160 Faverney (Haute-Saone), France **/Sexual difficulties among convalescing alcoholics: interest in prazepam treatment in 30 cases./** Troubles sexuels et postcure. Interet d'un traitement par prazepam: a propos de 30 observations. Psychologie Medicale. 12(10):2247-2254, 1980.

The treatment of sexual disturbances in convalescing alcoholics using prazepam was studied. Thirty male subjects were administered 20mg to 60mg of prazepam daily for a period of 6 months. Personal questionnaires monitored changes in the Ss' sexual disturbances. Results indicate that the majority of patients recovered sexual functions without the usual side-efects of other benzodiazepines. 4 references. (Journal abstract modified)

003297 Branconnier, Roland J.; Cole, Jonathan O.; Ghazvinian, Sasan. Boston State Hospital, Boston, MA **The therapeutic profile of mianserin in mild elderly depressives.** Psychopharmacology Bulletin. 17(1):129-131, 1981.

The therapeutic profile of mianserin was assessed in a sample of 75 elderly patients with mild to moderate depressive symptomatology and impaired cognitive function. All patients were assigned to a single blind, placebo run-in period of 7 days. During the second week of the study, patients were assigned to receive mianserin, amitriptyline, or placebo for the remainder of the 35 day trial. Mianserin was found to be an effective antidepressant comparable in therapeutic efficacy to the tricyclic antidepressants. Furthermore, it produces no significant cognitive impairment, alteration of cardiovascular function, or anticholinergic side-effects compared to the tricyclic antidepressants. 9 references. (Author abstract modified)

003298 Breuning, Stephen E.; Ferguson, Donald G.; Cullari, Salvatore. Psychological and Research Services, Coldwater Regional Center for Developmental Disabilities, Coldwater, MI **Analysis of single-, double-blind procedures, maintenance of placebo effects, and drug-induced dyskinesia with mentally retarded persons -- brief report.** Psychopharmacology Bulletin. 17(1):122-123, 1981.

The importance of reliability checks, placebo conditions, and double-blind conditions in assessing medication effects with institutionalized mentally retarded samples was investigated. Ss were 10 institutionalized mentally retarded prsons receiving thioridazine, chlorpromazine, or haloperidol. Ss were randomly assigned to one of four sequences of conditions manipulating expectancies and reinforcements. Significant differences due to staff expectancies, and loss of reinforcement (attention to residents at medication time) were found, demonstrating the importance of using reliability checks, placebo conditions, and double-blind conditions in assessing medication effects with mentally retarded persons. Clinical implications are discussed. 1 reference. (Author abstract modified)

003299 Brinkman, Samuel David. University of Houston **Lecithin and memory training in Alzheimer's disease. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3223-B, 1981. Ann Arbor, Univ. Microfilms No. 8104560, 108p., 1980.

The effects of lecithin and cognitive training procedures on memory performance, EEG, and regional cerebral blood flow (rCBF) were investigated in 10 patients (54 to 73 years old) diagnosed clinically as having mild to moderate Alzheimer's disease. The first phase of the study was a double-blind crossover design with a placebo control. No significant letithin/training effect on memory performance, EEG, or rCBF was found. During the second phase of the study, eight of these patient were followed in a series of single case studies to determine whether a longer period of lecithin therapy would facilitate memory functioning. Memory training was administered under placebo condition as well. A significant training effect on memory performance was found. Results are discussed in the context of the nature of the cholinergic deficit in Alzheimer's disease and the role of memory training procedures in elderly demented individuals. (Journal abstract modified)

003300 Broeker, Harald; Muller, Detlef; Muller, Jutta; Walther, Heinz. Neurologisch-Psychiatrische Kl., Med. Akad. Carus," Fetscherstr. 74, DDR-8019 Dresden, German Democratic Republic **/On the anticonvulsant blood level in therapy resistant epileptic patients./** Zum Antikonvulsivablutspiegelverhalten therapieresistenter Epilepsiepatienten. Psychiatrie, Neurologie und Medizinische Psychologie. 32(9):541-549, 1980.

Anticonvulsant blood level studies were conducted in 146 therapy resistant patients who had experienced severe epileptic attacks. Among the patients, most of whom were adults and were treated with combinations of drugs, only 24% reached the assumed normal phenytoin range, while 69% remained below it. With the administration of phenobarbital, however, 50% reached the therapeutic range, and only 14% reached the lower limiting value. Only in the latter group was an insufficient intake of drugs assumed. When diphenylhydantoin was administered, difficulties in determining the plasma water range were encountered. In practice, blood level determination was seen as having special value for detecting mild anticonvulsant intoxications and wrong drug dosages. 12 references. (Journal abstract modified)

003301 Calandra, C.; Drago, F.; Filetti, S. Clinica Psichiatrica, Facolta di Medicina e Chirurgia, Universita, Catania, Italy /**On a case of memory disturbances treated with vasopressin.**/ Su un caso con turbe mnestiche trattato con vasopressina. Minerva Psichiatrica. 21(1):63-66, 1980.

The treatment of memory disturbances using vasopressin was studied. The subject was a 29-year-old female, suffering from amnesia and hypothalamic disorders. The treatment consisted of the administration of five units of vasopressin daily for 10 days. Later, the subject was administered the Wechsler-Bellevue Intelligence Scale and the Benton Retention Test. Results show that therapy with vasopressin restored memory consolidation and learning processes. It is concluded that the physiological role of the drug was confirmed. 9 references. (Journal abstract modified)

003302 Casey, Daniel E.; Gerlach, Jes; Magelund, Gerhard; Christensen, Torben Rosted. Dept. of Psychiatry, VA Medical Center, Portland, OR 97201 **Dopaminergic and GABAergic aspects of tardive dyskinesia.** Psychopharmacology Bulletin. 17(1):49-50, 1981.

Clinical studies of the influence of dopaminergic and GABAergic drugs on tardive dyskinesia are reviewed. It is claimed that drugs with known, specific effects constitute the best method for investigation of the pathogenesis of tardive dyskinesia. Thus far, sulpiride (a selective antagonist to type 2 dopamine receptors), oxiperomide (another D2 dopamine receptor blocker), gamma-acetylenic GABA (a catalytic inhibitor of GABA transaminase), and muscimol (a GABA receptor agonist) have been demonstrated to reduce tardive dyskinesia. 13 references. (Author abstract modified)

003303 Castaigne, P.; Lapiane, D.; Morales, R. Clin. Malad. Systeme Nerv., Hopital de la Salpetriere, Paris, France /**Clomipramine treatment of pain from lesions of the peripheral nervous system: 30 case studies.**/ Traitement par la clomipramine des douleurs des neurophathies peripheriques. 30 observations. Therapeutique. 8:843-845, 1979.

Evidence is presented that clomipramine used alone is an effective analgesic against organic pain due to a lesion of the peripheral nervous system, particularly postherpetic pain. The quality of the drug response was related to the dosage and to the degree of tolerance. Fluohydrocortisone was the most powerful drug against orthostatic hypotension, the chief cause of limitation of treatment. No complications were seen, even in very elderly patients. (Journal abstract modified)

003304 Chojnacki, Michael; Mann, Edward; Shvartsburd, Alla; Wingfield, Cecil W.; Campbell, Katherine; Smith, Robert C. Smith: Texas Research Institute of Mental Sciences, 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Comparison of standard and Holter-monitored EKGs in a patient treated with several antidepressants.** Research Communications in Psychology, Psychiatry and Behavior. 6(1):103-111, 1981.

Cardiovascular effects and plasma levels of three antidepressant drugs were assessed by both standard and 24 hour Holto monitored EKGs in a patient with preexisting cardiac disease. Both EKG measurment procedures showed similar effects of the antidepressants on most EKG parameters; there was a small increase in the patient's heart rate. Only with the 24 hour EKG could the effects of antidepressants on arrhythmias and ectopic beats be accurately assessed. All three antidepressants had quinidine-like effects, reducing the number of ectopic beats.

003305 Chouinard, Guy; Annable, Lawrence; Ross-Chouinard, Andree; Olivier, Mireille; Fontaine, Francine. Dept. of Psychiatry, McGill University, Montreal, Canada **A double-blind, placebo-controlled study of piracetam in elderly psychiatric patients.** Psychopharmacology Bulletin. 17(1):129, 1981.

A double-blind, placebo controlled study of the efficacy of piracetam with elderly psychiatric patients with mild impairment of brain function, is described. The 60 patients were randomly assigned to one of three drug treatments: placebo, piracetam 2.4g per day, or piracetam 4.8g per day. During the 12 week study period, patients treated with either dose of piracetam had significantly higher mean scores on the Nurse's Improvement Scale than control Ss. On the WAIS, patients treated with the lower dose of piracetam did significantly better than the placebo or high dose drugs. Similarly, on the Wechsler Memory Scale, the lower dose group tended to show significant improvement relative to the placebo and high dose groups. 2 references. (Author abstract modified)

003306 Cohen, Nancy J.; Sullivan, Janette; Minde, Klaus; Novak, Carole; Helwig, Catherine. Psychiatric Research Unit, Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8 **Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children.** Journal of Abnormal Child Psychology. 9(1):43-54, 1981.

The effects of three modes of treatment of kindergarten aged hyperactive children were evaluated in relation to an untreated control group. The treatments were administered over a 3 month period and included: cognitive behavior modification, methylphenidate, and the two treatments combined. A followup assessment approximately 1 year later (at the end of the first grade) indicated that all the children became less symptomatic over time. Analyses of psychological, rating scale, observational, and interview data indicate that none of the treatments was significantly more effective than no treatment at all. 20 references. (Author abstract modified)

003307 Dam, Mogens. University Clinic of Neurology, Hvidovre Hospital, Copenhagen, Denmark **Recent advances in the treatment of epilepsy.** Acta Neurologica Scandinavica. 62(Suppl. 78):88-102, 1980.

Recent advances in the pharmacological treatment of epilepsy are discussed. Side-effects associated with the chronic use of traditional anticonvulsants (phenytoin, hydantoin, barbiturate derivatives) are summarized. Recent research into two newer antiepileptic drugs, carbamazapine and valproic acid, is reviewed in the areas of antiepileptic effect, basic human pharmacokinetics, interactions, and relation of plasma drug level and therapeutic effect. Special problems are delineated including dosing problems with phenytoin and problems related to treatment of epilepsy during pregnancy. A list of drugs, in order of effect on the different types of seizure disorder, is provided. 76 references.

003308 Diamond, Ronald J.; Brooner, Robert K.; Lowe, Donald; Savage, Charles. Center for Health Sciences, 600 Highland Avenue, Madison, WI 53792 **The use of minor tranquilizers with jail inmates.** Hospital & Community Psychiatry. 32(1):40-43, 1981.

The use of minor tranquilizers with jail inmates is discussed with reference to a survey of jail mental health services in 58 California counties and a medication linked group therapy program in one county jail. The decision whether or not to prescribe minor tranquilizers may present an apparent dilemma to mental health professionals working with inmate populations: by dispensing anxiety reducing drugs, they may help the inmate cope with existing hardship conditions, but they may also contribute to drug dependency. Data for 38 counties reveal a general distrust of minor tranquilizers as a therapeutic modality; with 34 respondents indicated that policies were restrictive with tranquilizers being seldomly prescribed. A medication linked group therapy program in the Santa Clara jail is described. After 7 months, it was decided to discontinue the policy of prescribing medication as part of the group. Although this policy change initially evoked anger and many members had initially maintained they attended sessions only to receive the drugs, only one group member dropped out after the change. It is suggested that with consistent prescribing policies and concurrent group therapy, minor tranquilizers can be important transitional objects toward more collaborative therapeutic encounters within the jail setting. 9 references. (Author abstract modified)

003309 Eisler, T.; Teravainen, H.; Nelson, R.; Krebs, H.; Weise, V.; Lake, C. R.; Ebert, M. H.; Whetzel, N.; Calne, D. B. Calne: Bldg. 10, Room 6D20, NIH, Bethesda, MD 20205 **Deprenyl in Parkinson disease.** Neurology. 31(1):19-23, 1981.

A double-blind, clinical comparison of (-)deprenyl a specific monoamine oxidase subtype-B inhibitor, with placebo with 11 parkinsonian patients, in which the efficacy of 10mg daily was studied over 4 weeks, is described. In four cases, the clinical score for parkinsonian deficits improved during deprenyl therapy, and in five cases it deteriorated. There was no change in one patient; two patients failed to complete the study. Deprenyl induced euphoria and insomnia. It is concluded that any advantages deriving from the use of (-)deprenyl in parkinsonism are limited, and probably dominated by its elevation of mood. Biochemical analysis failed to reveal any significant increase in platelet or plasma catecholamine concentrations during deprenyl therapy. There was, however, a significant decrease in plasma epinephrine and platelet monoamine oxidase activity. 20 references. (Author abstract modified)

003310 Elkins, Robert; Rapoport, Judith; Zahn, Theodore; Buchsbaum, Monte; Weingartner, Herbert; Kopin, Irwin; Langer, Dennis; Johnson, Chris. Rapoport: Bldg. 10, Rm. 3N204, NIMH, Bethesda, MD 20205 **Acute effects of caffeine in normal prepubertal boys.** Amercian Journal of Psychiatry. 138(2):178-183, 1981.

The cognitive and behavioral effects of caffeine were compared to those of amphetamine in 19 prepubertal boys. Ss were observed following administration of a single dose of placebo, 3mg/kg of caffeine, and 10mg/kg of caffeine in a double-blind, crossover design. Caffeine produced increased vigilance and decreased reaction time, as does amphetamine. Unlike amphetamine, the higher dose of caffeine did not have a calming motor effect but increased motor activity. Separate biological systems, therefore, may be differentially affected by the two substances. 30 references. (Author abstract modified)

003311 Esteban, Angel; Mateo, Dolores; Gimenez-Roldan, Santiago. Laboratory of Clinical Neurophysiology, Ciudad Sanitaria Provincial, Dr. Esquerdo, 46, Madrid-30, Spain **Early detection of Huntington's disease. Blink reflex and levodopa load in presymptomatic and incipient subjects.** Journal of Neurology, Neurosurgery, and Psychiatry. 44(1):43-48, 1981.

In a study of early detection of Huntington's disease, 17 Huntington's disease descendants were observed for the presence of dyskinesias and the blink reflex pattern before and after a levodopa load, and were compared to four incipient cases and normal control Ss. The R2 response on the blink reflex was found to be abnormal in 7 of the 17 Huntington's disease descendants. Such abnormalities were present in four untreated Ss and in three other Ss after administration of a single oral dose of levodopa/carbidopa. An increase in latency and differential latency (four cases), or an increase in a single one of these parameters (three cases) were the abnormalities found, resembling findings in four incipient cases detected during routine family surveys. Continuous administration of levodopa/carbidopa over a 10 to 20 day period did not induce new characteristics in the blink reflex, nor did it increase those detected previously, and no case developed chorea. It is suggested that the analysis of the blink reflex after a single oral levodopa/carbidopa dosage could provide an objective and quantifiable method for the detection of individuals at-risk for Huntington's disease. 13 references. (Author abstract modified)

003312 Ferguson, H. B.; Pappas, B. A.; Trites, R. L.; Peters, D. A. V.; Taub, H. Dept. of Psychology, Carleton University, Ottawa, Ontario K1S 5B6, Canada **Plasma free and total tryptophan, blood serotonin, and the hyperactivity syndrome: no evidence for the serotonin deficiency hypothesis.** Biological Psychiatry. 16(3):231-238, 1981.

Total and free plasma tryptophan and plasma cortisol levels were determined for children diagnosed as hyperactive or learning disabled and in normal siblings of these Ss. No differences were observed among the groups on any of the dependent variables related to a number of parameters measured for the hyperactive children, such as degree of hyperactivity, presence of food allergies, favorable response to methylphenidate, and brain dysfunction. Moreover, in further comparisons, no differences were found between hyperactive and age matched controls on these variables, as well as blood serotonin, nor were any differences found for a group of hyperactive children between placebo and methylphenidate trials. These data do not support earlier suggestions of a serotonin deficiency in hyperactive children. 26 references. (Author abstract)

003313 Fontan, Michel; Piquet, Jean-Michel; Delot, Daniel. Centre Hospitalier Regional, place de Verdun, F-59037 Lille Cedex, France **/Polygraphic study of night sleep under the effects of minaprine./** Etude polygraphique du sommeil de nuit sous minaprine. Psychologie Medicale. 12(13):2809-2818, 1980.

Polygraphic tests were conducted to determine the effect of minaprine on sleep. Five Ss were given 100mg of minaprine every morning and evening for 15 days. Prior to the experiment, two of the Ss were satisfied with their sleep, one S was usually satisfied with his sleep; one S was a sleepwalker, and one S had generalized sleep problems. Three polygraphs were done for each S over the course of the experiment, and slow, rapid, and intermediate sleep were distinguished. Results show improved sleep organization in four out of five Ss. 34 references. (Journal abstract modified)

003314 Froscher, W.; Eichelbaum, M.; Gugler, R.; Hildenbrand, G.; Penin, H. Dept. of Neurology and Epileptology, University of Bonn, D-5300 Bonn 1, West Germany **A prospective randomised trial on the effect of monitoring plasma anticonvulsant levels in epilepsy.** Journal of Neurology. 224(3):193-201, 1981.

The contribution to therapeutic effects of antiepileptic drugs of monitoring plasma anticonvulsant levels was assessed in a prospective randomized trial employing 127 epileptic outpatients as Ss. Ss were assigned to one of two groups. Plasma levels of Group A were reported to the treating physician, who attempted to keep the plasma levels within the therapeutic range. Plasma levels of Group B were not reported to the treating physician. During the one year study period, data from 105 patients were collected. No significant differences in therapeutic results of anticonvulsant therapy were found between the two groups. Thus, knowledge of plasma levels of antiepileptic drugs did not further improve therapeutic results. 11 references. (Author abstract modified)

003315 Fukuhara, Tomokazu; Kawahara, Ryuzo; Hazama, Hidebumi. Dept. of Neuropsychiatry, Tottori University, School of Medicine, Tottori, Japan **Serum concentration and clinical effect of antiepileptics.** Kyushu Neuro-Psychiatry. 25(3-4):212-218, 1979.

Serum concentration of antiepileptics in 78 ambulant epileptic patients was measured by gas chromatography. The results were as follows: the serum level of sodium valproate decreased slightly 4 to 5 months after the the combined administration of sodium valproate with the antiepileptics phenobarbital, diphenylhydantoin, or carbamazepine; and the serum levels of phenobarbital, diphenylhydantoin, and carbamazepine also decreased. The number of cases in which the serum level of phenobarbital exceeds 30mg/ml were larger in the phenobarbital plus primidone group than in the phenobarbital or primidone group. However, no significant discrepancy was found in either case. Between the dose and serum concentration of phenobarbital there was a statistically linear correlation. The level/dosage ratios of diphenylhydantoin, carbamazepine, and sodium valproate were larger in the excellently controlled general motor seizure group than in the moderately controlled general motor seizure group. The level/dosage ratios of diphenylhydantoin, carbamazepine, and sodium valproate were larger in the moderately controlled psychomotor seizure group than in the uncontrolled psychomotor seizure group. The results illustrate the clinical effects and interactions of antiepileptic drugs in response to drugs. 20 references. (Author abstract modified)

003316 Gannaway, D. J.; Mawer, G. E. Dept. of Pharmacology, Materia Medica and Therapeutics, Medical School, University of Manchester, Manchester M13 9PT, England **Transfer from multiple to single antiepileptic drug therapy.** Lancet. No. 8213:217, 1981.

Evidence is reported for the successful management of most newly diagnosed epileptic patients with a single drug. The seizure frequency of patients on multiple drug therapy was compared with that of patients being treated with phenytoin alone. Comparable results were obtained with most patients, and it is concluded that many poorly controlled epileptic patients gain little extra benefit from multiple drug therapy. 3 references.

003317 Gold, Mark S.; Pottash, A. L. C.; Sweeney, Donald R.; Kleber, Herbert D. Yale University School of Medicine, Dept. of Psychiatry, New Haven, CT 06510 **Efficacy of clonidine in opiate withdrawal: a study of thirty patients.** Drug and Alcohol Dependence. 6(4):201-208, 1980.

Evidence is presented on the efficacy of clonidine in reducing objective signs and subjective symptoms of opiate withdrawal in 30 hospitalized addicts. The reduction was observed in an acute first dose study using a placebo controlled double-blind crossover trial. In an open trial, with repeated administration clonidine suppressed opiate withdrawal signs and symptoms and allowed all of the patients to detoxify successfully from chronic addiction. These data support a release from chronic opiate induced noradrenergic inhibition producing noradrenergic hyperactivity as the pathophysiological substrate for opiate withdrawal. It appears that clonidine replaces opiate mediated inhibition with alpha-2 mediated inhibition of noradrenergic nuclei. 20 references. (Author abstract modified)

003318 Goode, David J.; Meltzer, Herbert Y.; Fang, Victor S. Dept. of Psychiatry, Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, NC 27103 **Increased serum prolactin levels during phenothiazine and butyrophenone treatment of six postpartum women.** Psychoneuroendocrinology. 5(4):345-351, 1980.

Serum prolactin levels of six women who developed psychoses during the postpartum period and were treated with neuroleptic drugs, were found to be higher than those of a group of nonpostpartum women of comparable age treated with similar doses of these drugs. The magnitude of the neuroleptic induced elevations in serum prolactin diminished with time during the postpartum period and returned to that found in nonparturient drug treated females approximately 120 days postpartum. A similar increased responsiveness of the hypothalamic/pituitary axis controlling prolactin secretion in postpartum females is manifested by the suckling response and increased prolactin response to thyrotrophin releasing hormone (TRH). The time course of normalization of these enhanced endocrine responses is roughly similar to that found for normalization of the prolactin response to neuroleptic drugs. A common mechanism may underlie each of these phenomena. 16 references. (Author abstract modified)

003319 Gopinathan, G.; Teravainen, H.; Dambrosia, J. M.; Ward, C. D.; Sanes, J. N.; Stuart, W. K.; Evarts, E. V.; Calne, D. B. Calne: NINCDS, Building 10, Room 6D20, NIH, Bethesda, MD 20205 **Lisuride in parkinsonism.** Neurology. 31(4):371-376, 1981.

The actions of lisuride, a dopaminergic ergot derivative, were studied in 20 parkinsonian patients. When the dose was increased gradually, most patients tolerated up to 5mg daily. Clinical assessment and objective, computer assisted evaluation revealed improvement in akinesia, rigidity, and tremor. Adverse reactions were similar to those seen with levodopa and bromocriptine, but somnolence tended to occur more often with lisuride. Clinical implications of these data are discussed. 14 references. (Author abstract modified)

003320 Green, Leonard; Warshauer, David. Dept. of Psychology, Washington University, St. Louis, MO 63130 **A note on the hyperactivity with reference to the rate-dependency effect of drugs.** Journal of Nervous and Mental Disease. 169(3):196-198, 1981.

Research findings that administration of stimulant drugs to hyperactive children often, paradoxically, leads to a decrease in their excessive motor activity are reviewed and various explanations are considered. Emphasis is on the rate dependency hypothesis, which states that the effect of a given drug is determined by the baseline rate of behavior emitted by the S. Amphetamines decrease response output under schedules maintaining high response rates, but increase response output under schedules maintaining low response rates. In hyperactive children, when baseline motor activity is high, the stimulant drug should, therefore produce a reduction in such behavior. It is also suggested that greater emphasis be placed on reporting individual data, and that more detailed specification be made of the target responses. 30 references. (Author abstract modified)

003321 Greenhill, Laurence L.; Barmack, Joseph E.; Spalten, David; Anderson, Mary; Halpern, Frieda. New York Psychiatric Institute, New York, NY **Molindone hydrochloride in the treatment of aggressive, hospitalized children.** Psychopharmacology Bulletin. 17(1):125-127, 1981.

The safety and effectiveness of molindone hydrochloride (Moban) treatment of hospitalized preschool (ages 6 to 11 years) children who meet DSM-III criteria for undersocialized conduct disorder with aggressivity, severe type, were assessed. The nature of the drug's therapeutic effects and treatment emergent symptoms (weight changes, presence of involuntary movement disorders, sedation, attentional deficits, and prolactin secretory changes) were followed. Aggression ratings were improved for five of the six Ss, with mild but acceptable treatment emergent symptoms, following Moban treatment. 12 references. (Author abstract modified)

003322 Haldeman, S.; Goldman, J. W.; Hyde, J.; Pribram, H. F. W. Dept. of Neurology, University of California, Irvine Medical Center, 101 City Drive South, Orange, CA 92668 **Progressive supranuclear palsy, computed tomography, and response to antiparkinsonian drugs.** Neurology. 31(4):442-445, 1981.

Findings on computed tomography in three cases of progressive supranuclear palsy are reported, and amelioration of some symptoms by anticholinergic medication is described. Three patients with progressive supranuclear palsy demonstrated atrophy of the midbrain, pons, cerebellum, and cerebral hemispheres by computed tomography with horizontal, sagittal, and coronal reconstruction. Benztropine therapy resulted in improvement of speech and gait without significantly affecting the vertical gaze palsy. Benztropine had to be discontinued because of mental confusion in one patient. Additional improvement was not obtained with amantadine, and in one case symptoms became worse. 15 references. (Author abstract modified)

003323 Hefti, Franz; Melamed, Eldad. Laboratory of Neuroendocrine Regulation, Massachusetts Institute of Technology, Cambridge, MA 02139 **L-DOPA's mechanism of action in Parkinson's disease.** Trends in NeuroSciences. 3(10):229-231, 1980.

The mechanisms of L-DOPA action in Parkinson's disease is reviewed, with special emphasis on the most important phenomenon that limits L-DOPA's use in the treatment of parkinsonism – its declining effectiveness. Declining efficacy and adverse side-effects such as dyskinesias and psychiatric reactions, are phenomena that, after several years, limit L-DOPA's use in the therapy of Parkinson's disease, and can occur together or independently of each other in different patients. Three possible mechanisms underlying the declining effectiveness of L-DOPA therapy are noted: 1) that only insufficient amounts of L-DOPA are decarboxylated to dopamine after large reductions in DOPA decarboxylase activity; 2) that chronic treatment with L-DOPA has a toxic influence on dopaminergic neurons and could accelerate the progression of Parkinson's disease; and 3) that alteration in receptor sensitivity might take place. 18 references.

003324 Henry, Jean-Francois; Hrdina, Pavel D.; Altamura, Carlo; Rovei, Vincenzo; Gomeni, Roberto; Hervy, Marie-Pierre; Forette, Francoise; Morselli, P. L. Dept. de Recherche Clinique, S.N.C. Lers-Synthelabo, 58, rue de la Glaciere, F-75013 Paris, France **/Pharmacokinetics of amitriptyline, imipramine, and maprotiline in the elderly./** Pharmacocinetique de l'amitriptyline (AMI), l'imipramine (IMI) et la maprotiline (MAP) chez le sujet age. Psychologie Medicale. 12(11):2389-2394, 1980.

Pharmacokinetics of amitriptyline, imipramine, and maprotiline in the elderly were investigated. The Ss, between ages 75 and 83, received a single dose of 125mg of amitriptyline, 125mg of imipramine, and 175mg of maprotiline. The results of the observations of the elderly were compared to those obtained in previous research with young Ss. In comparison with values reported in young adults, a reduction of plasmatic clearances and an increase in bioavailability of imipramine and amitriptyline were observed in the elderly. The rate of absorption of the three compounds was the same in young and elderly patients; the rate of metabolite formation was found to be slower in the elderly. Alterations in heartrates, blood pressure, or EKG occurred in all subjects with amitriptyline, but not with imipramine or maprotiline. 10 references. (Journal abstract modified)

003325 Hogben, George L.; Cornfield, Richard B. 12 Rockbridge Rd., Rye, NY 10580 **Treatment of traumatic war neurosis with phenelzine.** Archives of General Psychiatry. 38(4):440-445, 1981.

The treatment of traumatic war neurosis with phenelzine is reported. Five patients with traumatic war neurosis had favorable therapeutic responses to phenelzine sulfate. These patients did not respond to multiple previous therapeutic trials with antipsychotics, tricyclic antidepressants, and psychotherapy with or without medication. With phenelzine, the patients felt calmer and stopped having nightmares and flashbacks of traumatic war material. Startle reactions and aggressive, violent outbursts also ceased. 25 references. (Author abstract)

003326 Il'ina, N. A.; Antipova, R. I.; Khokhlov, A. P. Lab. nasledstvennoy patologii nervnoy sistemy I Moskovskogo meditsinskogo instituta im I. M. Sechenova, Moskva, USSR **/The use of lithium carbonate for treating Kugelberg-Welander spinal amyotrophy patients./** Primeneniye uglekislogo litiya dlya lecheniya spinal'noy amiotrofii Kugel'berga-Velandera. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(11):1657-1660, 1980.

The use of lithium carbonate for treating Kugelberg-Welander spinal amyotrophy patients was studied in 11 men and 9 women (12 to 42 years old). All Ss had clear clinical and electromyographic symptoms of the disease. The use of lithium carbonate caused positive clinical and biochemical changes. Results suggest that lithium carbonate, which is an inhibitor of adenylcyclase, should be used medicinally because of the disturbance of the metabolism of 3',5'-adenosine monophosphate in patients with Kugelberg-Welander's amyotrophy. These results show that the drug stabilizes the pathological process. 13 references. (Journal abstract modified)

003327 Jansen, W.; Bruckner, G. W. Altenkrankenhaus, Nurnberg, West Germany **/Treatment of organic brain disturbances in elderly patients. A clinical double-blind study with macromolecular organ lysates (cytoplasmatic therapy according to Theurer)./** Behandlung hirnorganischer Storungen von Alterspatienten. Eine klinische Doppelblindstudie mit makromolekularen Organlysaten (Zytoplasmatische Therapie nach Theurer). Neurologie und Psychiatrie fur die Praxis. 5:214-220, 1979.

Double-blind studies on the therapeutic effect of macromolecular cytoplasmatic substances for the treatment of organic brain disturbances in elderly patients are reported. Such substances are seen as causing physiological stimulation or cerebral protein synthesis. Theoretical considerations on the mechanisms of action of cytoplasmatic substances are offered. In the cases represented, a marked improvement of cerebral capacity was recorded, thus giving new hope to the elderly patient with cerebral failure. (Journal abstract modified)

003328 Jardim, Edymar; Takayanagui, Osvaldo M. Faculdade de Medicina de Ribeirao Preto, Av. 9 de Julho 980, 14100 Ribeirao Preto, Sao Paulo, Brazil **/Epilepsy and chronic Chagas' disease./** Epilepsia e doenca de Chagas cronica. Arquivos de Neuro-Psiquiatria. 39(1):32-41, 1981.

A total of 167 epileptics in two groups, one consisting of 44 Ss with chronic Chagas' disease, were studied in order to establish a causal relationship between chronic Chagas' disease and the epileptic syndrome, and to evaluate therapeutic results with anticonvulsant drugs. Origin, sex, age, onset of epilepsy, and types of seizures were examined for all Ss. Results show that the chagasic patients have a later onset of seizures than do the control group, and they exhibit a predominance of autonomic partial seizures. The neurological examinations and cerebrospinal fluid tests reveal moderate rates of disturbances, which are high enough to characterize a neurological syndrome. The EEG recordings for 15 of the 44 cases reveal patterns of diffuse cerebral damage in half of the patients. The pharmacological control of epileptic seizures in Chagas' disease requires greater quantities of anticonvulsant drugs than do other types of epilepsy. 34 references. (Journal abstract modified)

003329 Jasinski, Donald R. NIDA, Addiction Research Center, Baltimore, MD **Clinical pharmacology of mixed agonist-antagonist drugs.** Psychopharmacology Bulletin. 17(1):85-86, 1981.

The clinical pharmacology of mixed agonist/antagonist drugs is briefly reviewed, and the utility of buprenorphine, a partial agonist of the morphine type, in treating narcotic addiction is described in relation to structure/activity relations and clinical acceptance. Buprenorphine produces methadone-like and morphine-like subjective effects that are acceptable to addict/patients. However, buprenorphine does not produce significant methadone-like or morphine-like physical dependence and toxicity. 5 references. (Author abstract modified)

003330 Kanto, J.; Iisalo, E.; Kangas, L.; Valovirta, E. Dept. of Anaesthesiology, Turku University Central Hospital, Kiiamyllynkatu 8, SF-20520 Turku 52, Finland **A comparative study on the clinical effects of rectal diazepam and pentobarbital on small children. Relationship between plasma level and effect.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 18(8):348-351, 1980.

The clinical effects of rectal diazepam (5mg) and pentobarbital (60mg) were studied in 75 juvenile surgical patients. No difference in demeanor in the anesthetic room, preoperative emesis, response to venepuncture, degree of salivary suppression, postoperative state in the recovery room, or postoperative emetic effects were found between the two drug groups. Plasma concentrations of diazepam and its active metabolites were not significantly correlated with clinical effects of diazepam, but a weak positive correlation between plasma pentobarbital concentrations and clinical effects was found. Plasma concentrations of pentobarbital and benzodiazepine showed wide interindividual variation, indicating irregular rectal drug absorption. 19 references. (Author abstract modified)

003331 Klapetek, J. Pavlovova 13, 775 00 Olomouc, Czechoslovakia **/The tranquilizer Demetrin (prazepam)./** Trankvilizer Demetrin (prazepam). Ceskoslovenska Neurologie a Neurochirurgie. 43(1):51-58, 1980.

The effects of the tranquilizer prazepam, sold in Europe under the commercial name Demetrin, were studied in 115 cases of patients suffering from epilepsy. The results were often surprisingly good. Two cases of young patients are described, with one case of the treatment of migraine with prazepam. It is confirmed that in the treatment of neurotic difficulties with symptoms of anxiety and depression, prazepam is qualitatively different from diazepam and chlordiazepoxide. The biochemical and pharmacological properties of prazepam are described. 37 references.

003332 Kolin, Irving S.; Linet, Otto I. 1315 South Orange Ave., Orlando, FL 32806 **Double-blind comparison of alprazolam and diazepam for subchronic withdrawal from alcohol.** Journal of Clinical Psychiatry. 42(2):169-173, 1981.

The efficacy and safety of a new triazolobenzodiazepine, alprazolam, was compared to diazepam in 46 alcoholics in a double-blind study. The drugs were administered for 21 days starting on the fifth day after the last drink. The mean optimal daily oral dose of alprazolam was 2.2mg and that of diazepam was 20.2mg. Alprazolam was as effective as diazepam was in the relief of anxiety as measured by the Hamilton Anxiety Rating Scale, Physician's Global Impressions, Patient's Global Impressions, Hopkins Symptom Checklist, and Target Symptoms Record. At the end of the trial 95% of the patients in both groups experienced moderate to marked therapeutic effect and felt much or very much better as compared to the beginning of the study. The number of side-effects was similar in both groups and they were mostly described by patients as mild. 14 references. (Author abstract)

003333 Lambie, D. G.; Johnson, R. H. Wellington Clinical School of Medicine, Wellington, New Zealand **The effects of phenytoin on phenobarbitone and primidone metabolism.** Journal of Neurology, Neurosurgery, and Psychiatry. 44(2):148-151, 1981.

Serum concentrations of primidone and its metabolites, phenobarbitone and phenylethylmalonamide, were measured in 40 epileptic patients receiving treatment with primidone alone or primidone plus phenytoin. Serum phenobarbitone concentrations were also measured in 100 patients receiving phenobarbitone, alone or with phenytoin. Patients receiving either phenobarbitone or primidone in combination with phenytoin showed raised serum phenobarbitone concentrations. Phenytoin also caused raised phenobarbitone concentrations. Phenytoin also caused raised phenylethylmalonamide concentrations in patients on primidone. 9 references. (Author abstract)

003334 Lloyd, K. G.; Munari, C.; Worms, P.; Bossi, L.; Bancaud, J.; Talairach, J.; Morselli, P. L. Research Dept., Synthelabo-LERS, Paris F-75013, France **The role of GABA mediated neurotransmission in convulsive states.** Advances in Biochemical Psychopharmacology. 26:199-206, 1981.

Studies concerning the role of GABA mediated neurotransmission in convulsive states are reviewed. The anticonvulsant actions of drugs known to augment GABA synaptic activity either by being GABA receptor agonists (SL 76 002 and muscimol) or relatively specific inhibitors of GABA metabolism (gabaculine and amino-oxyacetic acid) are considered. New evidence that GABA neurons are dysfunctional in human epilepsy is presented as ascertained from the study of brain material removed during surgical resection for intractable epilepsy. Results indicate that glutamic acid decarboxylase activity and 3H-GABA binding sites are decreased in epileptic regions of many patients, as compared to nonepileptic brain regions. Increasing GABA mediated neurotransmission also plays a role in the mechanism of action of numerous anticonvulsants, either by direct GABA receptor stimulation or by inhibition of the metabolism of GABA. 41 references.

003335 Marcovici, Martin; O'Brien, Charles P.; McLellan, A. Thomas; Kacian, Jane. VA Medical Center, (158), University and Woodland Avenues, Philadelphia, PA 19104 **A clinical, controlled study of l-alpha-acetylmethadol in the treatment of narcotic addiction.** American Journal of Psychiatry. 138(2):234-236, 1981.

A comparison was made of the clinical effectiveness of l-alpha-acetylmethadol (LAAM) and methadone in the treatment of narcotic addiction. LAAM was as effective as methadone on all outcome measures, including length of stay in treatment. Two clinicopharmacologic properties of LAAM caused some patients to ask for a switch to methadone. These phenomena are described, along with their impact on the clinical effectiveness of the drug in dealing with opiate dependent patients. 17 references. (Author abstract modified)

003336 Markham, Charles H.; Diamond, Shirley G. Reed Neurological Research Center, University of California at Los Angeles, School of Medicine, Los Angeles, CA 90024 **Evidence to support early levodopa therapy in Parkinson disease.** Neurology. 31(2):125-131, 1981.

To investigate whether duration of disease or of levodopa treatment was responsible for gradual worsening of parkinsonian patients, 58 persons treated with levodopa were classified based on predopa disease duration. Data over 6 years of treatment show that disease duration is the determining factor in the gradual worsening of parkinsonian patients. Patients matched for disease duration had similar disability scores regardless of duration of therapy. Matched for therapy duration, patients with longer disease duration had consistently higher disability scores. Incidence of side-effects showed no differences between groups and did not increase over time. It is concluded that delaying therapy fails to improve disability in the early years of disease and does not confer any benefit in later years. 26 references. (Author abstract)

003337 Marzilli, Robert Alexander. University of Rhode Island **The effectiveness of imipramine in the treatment of enuresis: the significance of type of enuresis and reported level of sleep. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3188-B, 1981. Ann Arbor, Univ. Microfilms No. 8102334, 89p., 1980.

Factors which can influence the effectiveness of imipramine hydrochloride in the treatment of enuresis were evaluated with 28 male enuretics, aged 5 to 11 who were classified according to type of enuresis and reported level of sleep. Half the subjects were given the imipramine first, and the other half were given the placebo first. The results indicate that imipramine seems to reduce the number of wets under the conditions of the study regardless of type of enuresis or level of sleep, but it is most effective for enuretics who are deep sleepers. It does not appear that the imipramine's effectiveness is brought about by an increase in bladder capacity, since no significant change in the frequency of urination was shown for any of the groups while on the imipramine. It is felt, instead, that the efficacy of imipramine is due to physiological changes in the sleep stages as well as to its relaxing effect on the bladder musculature. (Journal abstract modified)

003338 McIntyre, Hugh B.; Firemark, Hugh M.; Cho, Arthur K.; Bodner, Lynn; Gomez, Miguel. Dept. of Neurology, Harbor-UCLA Medical Center, 1000 West Carson Street, Torrance, CA 90509 **Computer analyzed EEG in amphetamine-responsive hyperactive children.** Psychiatry Research. 4(2):189-197, 1981.

EEG frequency analysis and evoked potentials (EPs) of 27 hyperactive children were examined to determine which, if any, of these electrophysiological parameters might be useful for the selection of those children likely to respond to stimulant medication. The children were treated with placebo, d-amphetamine, and l-amphetamine in double-blind fashion and in random order. EEGs for frequency analysis, visual EPs and auditory EPs were obtained before and during treatment. Off medication, hyperactive responders to amphetamine had higher predominant beta frequency and shorter latencies of some EP waves than did nonresponders. Although the findings reported here would not select all responders, they would allow the exclusion of most nonresponders. 17 references. (Author abstract)

003339 Mikhaylova, N. M.; Severnyy, A. A. 3-e klinicheskoye otdeleniye Instituta psikhiatrii AMN SSSR, Moskva, USSR / **The effect of withdrawal from prolonged prophylactic treatment with lithium.**/ Effekt otmeny dlitel'noy profilakticheskoy litiyevoy terapii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(8):1216-1220, 1980.

The effect of withdrawal from prolonged prophylactic treatment with lithium was studied in two groups of patients, each consisting of 35 people (9 men and 26 women). One of these groups was used as a control group. In each group studied there were 15 cases of manic-depressive psychoses and 20 cases of attack-like schizophrenia. The development of these illnesses was monitored in one group following withdrawal from a prolonged and successful prophylactic intake of lithium drugs and compared to that in the control group, where the administration of lithium salts was not suspended. Results demonstrate a statistically significant increase of phase-like attacks as well as an increased number of hospitalizations due to lithium withdrawal. It is concluded that prolonged and continuous lithium prophylaxis is necessary even following complete remissions. 8 references. (Journal abstract modified)

003340 Mikkelson, Edwin; Lake, C. Raymond; Brown, Gerald L.; Ziegler, Michael G.; Ebert, Michael H. Lake: Dept. of Psychiatry, USUHS, Building B, Room 3049, 4301 Jones Bridge Road, Bethesda, MD 20014 **The hyperactive child syndrome: peripheral sympathetic nervous system function and the effect of d-amphetamine.** Psychiatry Research. 4(2):157-169, 1981.

Sympathetic nervous system function was evaluated in medication free hyperactive children by measuring plasma levels of norepinephrine (NE) and dopamine-beta-hydroxylase and then comparing the effects of two therapeutic doses of d-amphetamine to placebo in these patients. The medication free hyperactive patients and controls had similar NE levels and blood pressures while recumbent, and a similar increase in NE on standing, but the patients had a larger pressor response on standing. In the hyperactive patients, d-amphetamine significantly increased blood pressure, pulse rate, and NE levels. The change in NE levels correlated with the change in amphetamine levels. The medication free patients, when more anxious, had higher plasma NE levels. 54 references. (Author abstract)

003341 Montplaisir, J.; Saint-Hilaire, J. M.; Walsh, J. T.; Laverdiere, M.; Bouvier, G. Centre d'etude du sommeil, Hopital due Sacre-Coeur, Montreal, Montreal, Quebec H4J 1C5, Canada **Naloxone and focal epilepsy: a study with depth electrodes.** Neurology. 31(3):350-352, 1981.

The effects of naloxone were studied in five patients with focal epilepsy who had electrodes implanted in cortical and subcortical structures. There were no changes in interictal spike activity, responses to electrical stimulation, or frequency of spontaneous seizures. These results indicate that naloxone does not suppress interictal spike activity in any of the brain regions studied, whether or not these regions were within the epileptic zone. Furthermore, naloxone did not modify the response threshold of the cortical or limbic structures to electrical stimulation, nor did it interfere with the occurrence of seizures in one case of primary hippocampal epilepsy. Results do not support the hypothesis that opiate peptides play a major role in human focal epilepsy, at least in patients with an epileptic focus in the amygdala or hippocampus. 14 references. (Author abstract modified)

003342 Moore, Ray; Mills, Ivor H.; Forster, Alison. Dept. of Medicine, University of Cambridge, Aldenbrooke's Hospital, Cambridge C2B 2QQ, England **Naloxone in the treatment of anorexia nervosa: effect on weight gain and lipolysis.** Journal of the Royal Society of Medicine. 74(2):129-131, 1981.

The effects of a constant intravenous infusion of naloxone in doses ranging from 3.2 to 6.4mg/day were studied in a group of patients with anorexia nervosa. Patients showed a significantly greater weight gain during the infusion compared with the periods before and after naloxone. Plasma beta-hydroxybutyrate and nonestrified fatty acid levels fell during the infusion. It is suggested that, in man, naloxone has an antilipolytic effect in vivo. 5 references. (Author abstract)

003343 Morselli, Paolo L.; Franco-Morselli, Rosetta; Bossi, Laura. Dept. of Clinical Research, Synthelabo-LERS, 58 Rue de la Glasiere, F-75013 Paris, France **Clinical pharmacokinetics in newborns and infants: age-related differences and therapeutic implications.** Clinical Pharmacokinetics. 5(6):485-527, 1980.

Age related differences and therapeutic implications of clinical pharmacokinetics in newborns and infants are reviewed. The impact of development and pathology on the physiological variables determining drug disposition is described, and kinetic profiles of representative drugs used in the perinatal period and infancy are discussed. Data are reported which illustrate that the risk of both overdosing or underdosing drugs is greatly increased in the perinatal period. It is urged that therapeutic drug monitoring be regarded not as experimentation, but as an integral part of therapeutic intervention in the perinatal period. 304 references.

003344 Muller, Eckhart; Klagge, Eckehart; Stosch, Rainer. Nervenklinik, Medizinische Akademie Erfurt, Nordhauserstrasse 74, DDR-506 Erfurt, German Democratic Republic /**Investigation into the effect of flupherazine hydrochloride (Lyorodin) in children with behavioral disorders by means of psychophysiological parameters.**/ Uberprufung der Wirkung von Fluphenazinhydrochlorid (Lyorodin) bei verhaltensgestorten Kindern mittels psychophysiologischer Parameter. Psychiatrie, Neurologie und Medizinische Psychologie. 31(11):689-695, 1979.

In a group of 44 children with behavioral disorders, the mode of action of the phenothiazine preparation fluphenazine hydrochloride (Lyorodin) was tested by means of psychophysiological methods of measurement (critical flicker fuse frequency and measurement of response time). In some of the comparative examinations before and after administration of the drug, significant differences were found. A defined psychic stress resulted in changed measured values in both methods. Children with cerebral injuries showed a lower degree of reaction after the administration of the drug than childrn who were not encephalopathically affected. 36 references. (Journal abstract)

003345 Namba, Shimpei; Ishimitsu, Hiroshi; Nakasone, Susumu. Dept. of Neurosurgery, Iwakuni National Hospital, Iwakuni, Japan **Clinical significance of pyridoxine administration in L-dopa therapy of parkinsonism.** Brain and Nerve. 32(10):991-1000, 1980.

Twenty two patients with idiopathic parkinsonism were studied to assess the effects of administering pyridoxine in combination with the ongoing therapeutic regimen (L-dopa in combination with peripheral decarboxylase inhibitor). Administration of pyridoxine evoked oral dyskinesias and dyskinesias in the extremities in two patients. In three patients, pyridoxine prevented aggravation of the clinical symptoms of parkinsonism which might be expected following decrease in L-dopa/peripheral decarboxylase inhibitor. Pyridoxine increased the effectiveness of L-dopa/peripheral decarboxylase inhibitor in at least 6 of 18 patients. Pretreatment of rats with pyridoxine resulted in a 30% increase of dopamine in brain following L-dopa/peripheral decarboxylase inhibitor administration. Pyridoxine also elevated cerebrospinal fluid 5-hydroxyindoleacetic acid levels. 23 references. (Journal abstract modified)

003346 Neborsky, Robert; Janowsky, David; Munson, Ethan; Depry, Dennis. Dept. of Psychiatry, School of Medicine, University of California, La Jolla, CA 92093 **Rapid treatment of acute psychotic symptoms with high- and low-dose haloperidol: behavioral considerations.** Archives of General Psychiatry. 38(2):195-199, 1981.

The treatment of acute psychotic episode with low and high dose haloperidol was investigated in 20 psychiatric inpatients with diagnoses of schizophrenia, acute paranoid reaction, and manic-depressive illness/manic type (DSM-II criteria), using a rapid neuroleptization technique. A 6 day maintenance phase followed. Both groups improved at 1 hour, 1 day, and 7 days after starting treatment; and neither group differed as to degree of rapidity of symptom alleviation. Therefore, the results of the study do not give support for the administration of high doses of haloperidol to young, acutely psychotic inpatients with relatively good prognoses. 23 references. (Author abstract modified)

003347 Newhouse, Paul; Bridenbaugh, R. Harlan. Dept. of Psychiatry, Walter Reed Army Medical Center, Washington, DC 20012 **Pharmacologic characterization and lecithin treatment of a patient with spontaneous oral-facial dyskinesia and dementia.** American Journal of Psychiatry. 138(2):251-252, 1981.

A case history of a patient who developed a spontaneous oralfacial dyskinesia and mild dementia without exposure to neuroleptics is reported. Pharmacologic characterization led to selection of lecithin treatment, and improvement was noted not only in the movement disorder, but also in the patient's higher cognitive functioning. The enhancement of cholinergic function by lecithin is believed responsible for these effects. 10 references.

003348 Nieto, Dionisio. Service de Psychiatrie, Institut National de Neurologie et Neurochirurgie, Insurgentes Sur no. 3877, Mexico 22, D.F. Mexico /**Prussian blue: specific treatment of thallium, arsenic, industrial solvent intoxication, and other polyneuropathologies. A possible antipsychotic agent.**/ Bleu de Prusse: antidote specifiqu contre le thallium, l'arsenic, les solvants industriels et autres polynevropathies. Un agent antipsychotique possible. Psychologie Medicale. 12(11):2395-2397, 1980.

The use of Prussian blue as a possible antipsychotic agent in the treatment of thallium, arsenic, and industrial solvent intoxications was studied. Three cases of intoxication by thallium were treated with insoluble Prussian blue and demonstrated complete recuperation. One case of arsenic intoxication treated with the drug recovered completely over 3 months after the intoxication and after treatment with D-penicillamine failed. In six cases of polyneuropathology due to inhalation of industrial solvents, there was complete recuperation with Prussian blue. Favorable development with Prussian blue treatment in three cases of schizophrenia which had not responded to other treatment and five cases of schizophreniform mental disturbance were observed. 5 references. (Journal abstract modified)

003349 Nissen, G. Julius-Maximilians-Universitat Wurzburg, Josef-Schneider-Strasse 2, D-8700 Wurzburg, West Germany /**Treatment of anxiety in children and adolescents.**/ Zur Behandlung der Angst im Kindes- und Jugendalter. Zeitschrift fur Kinder- und Jugendpsychiatrie. 7(4):344-352, 1979.

Fear as a primeval phenomenon, an essential part of human development, is discussed in contrast to pathological anxieties as precursors and accompaniments of nearly all neurotic and psychotic illnesses. A combined approach is preferred when treating pathological anxieties in children and adolescents. Guidance or treatment of the parents, analytical psychotherapy or behavior therapy of the child or adolescent, and psychopharmacological treatment of the child or adolescent and occasionally the parents all are possible treatments. In the search for new anxiolytic drugs which have the strongest efficacy profiles and fewest side-effects, two open studies and one double-blind study with clobazepam (Frisium), oxprenolol (Trasicor) and nomifensine (Alival) were conducted. The results are discussed. 8 references. (Journal abstract modified)

003350 no author. Council on Scientific Affairs, AMA, 535 N. Dearborn St., Chicago, IL 60610 **Hypnotic drugs and treatment**

of insomnia. Journal of the American Medical Association. 245(7):749-750, 1981.

Reports of two expert committees (one at the National Institute on Drug Abuse and the other at the National Academy of Science Institute of Medicine) on the continued effectiveness of sedative/hypnotic drugs in treating insomnia are reviewed. The reports indicate that despite a variety of problems, these compounds still play an important adjunctive role in the managment of organic disease as well as in the management of insomnia. An effort to curtail the range of pharmacologic choices for use by the physician is criticized. More clinical and epidemiologic studies are recommended, along with emphasis on the diagnosis and management of insomnia and further investigation of the current scientific issues associated with sleep disorders. 5 references.

003351 Nuller, Yu. L.; Tochilov, V. A. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut imeni V. M. Bekhtereva, Leningrad, USSR **/The use of phenazepam in the treatment of psychotic patients./** Opyt primeneniya fenazepama dlya lecheniya bol'nykh psikhozami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(6):914-920, 1980.

Phenazepam, a potent anxiolytic tranquilizer, was used in the treatment of 173 mental patients suffering from schizophrenia, endogenous depression, involutional psychoses, and organic psychoses. In all cases the clinical picture was characterized by anxiety. In 37% of the patients the psychopathological symptomatology disappeared altogether, while in another 27% there was significant improvement. The best results were obtained in the treatment of anxious depressive states, depersonalization, and affective delusional states. The effectiveness of phenazepam against depersonalization is considered an indirect confirmation of the proposed theory that anxiety plays the main role in depersonalization. 8 references. (Journal abstract modified)

003352 Ochs, H. R.; Grube, E.; Greenblatt, D. J.; Arendt, R. Greenblatt: Div. of Clinical Pharmacology, Box 1007, New England Medical Ctr. Hospital, 171 Harrison Ave., Boston, MA 02111 **Intravenous quinidine in congestive cardiomyopathy.** European Journal of Clinical Pharmacology. 19(3):173-176, 1981.

A clinical trial of intravenous quinidine in congestive cardiomyopathy is described. Following a single intravenous quinidine infusion, left ventricular (LV) performance was evaluated in the eight Ss by echocardiography at multiple time points during the next 24 hours. Quinidine kinetics and protein binding were determined from multiple serum samples drawn for up to 36 hours after dosage. LV function was not impaired. Instead, quinidine transiently increased ejection fraction and rate of circumferential shortening. Endsystolic and enddiastolic LV internal diameter likewise were decreased. Blood pressure and ventricular rate were not significantly altered. Well controlled, slow intravenous infusion of quinidine does not impair LV performance and is safe for patients with compensated congestive cardiomyopathy. However, such patients may have reduced quinidine clearance and hence require lower doses than expected based on age and weight. 9 references. (Author abstract modified)

003353 Olanow, C. Warren; Finn, Andrew L. Dept. of Medicine (Neurology), Duke University Medical Center, Durham, NC 27710 **Phenytoin: pharmacokinetics and clinical therapeutics.** Neurosurgery. 8(1):112-117, 1981.

The pharmacokinetics and clinical therapeutics of the anticonvulsant medication phenytoin are described. Topics discussed include: bioavailability; volume of distribution; metabolism; clinical management; and side-effects. It is concluded that phenytoin is a highly effective anticonvulsant agent that is generally well tolerated and free of serious side-effects. Serum monitoring is necessary because of individual variations in the pharmacokinetic properties of phenytoin and the potential effects of other drugs and diseases. When a patient continues to have seizures with serum concentrations outside the therapeutic range, it is prefereable to adjust the dose of phenytoin rather than to substitute or add an additional medication. When phenytoin provides no seizure control, it should be discontinued gradually and a different anticonvulsant should be substituted rather than maintaining the patient on both medications. 50 references. (Author abstract modified)

003354 Oyewumi, L. K.; Lapierre, Y. D. Lapierre: Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, Ontario, Canada K1Z 7K4 **Efficacy of lithium in treating mood disorder occurring after brain stem injury.** American Journal of Psychiatry. 138(1):110-112, 1981.

A single case, double-blind design was used to assess the therapeutic value of lithium in the treatment of recurrent hypomania and depressive symptoms in a 21-year-old patient with brainstem injury. Lithium effectively controlled the patient's severe mood disturbance which occurred after cobalt radiation and invasive brain surgery for a medulloblastoma. The double-blind test period with placebo confirmed that response to lithium was not a placebo effect. Results suggest that in certain selected cases of organic brain disorder, lithium may be a valuable therapeutic agent. 10 references.

003355 Paulson, George W.; Lowery, Howard W.; Taylor, Gordon C. Ohio State University, 931 Chatham Road, Columbus, OH 43221 **Progressive supranuclear palsy: pneumoencephalography, electronystagmography and treatment with methysergide.** European Neurology. 20(1):13-16, 1981.

Clinical material from 15 patients with progressive supranuclear palsy (PSP) is described, and the value of pneumoencephalography (PEG) and electronystagmography (ENG) in confirming the diagnosis is discussed. PEG records of six patients revealed atrophy in the area of the pons and colliculi. ENG records of six patients (four of whom had received PEG) confirmed the defects in extraocular movement. Methysergide, which has been suggested as therapy for PSP, was administered to six patients, with no significant improvement in PSP symptoms. 7 references. (Author abstract modified)

003356 Petti, Theodore A.; Unis, Alan. Western Psychiatric Institute, 3811 O'Hara St., Pittsburgh, PA 15261 **Imipramine treatment of borderline children: case reports with a controlled study.** American Journal of Psychiatry. 138(4):515-518, 1981.

The borderline syndrome of childhood is examined and three case histories are presented to demonstrate its salient features. Each patient failed to benefit from intensive hospital treatment until imipramine (5mg/kg/day) was added to the treatment regimen. One child was treated in a double-blind, imipramine/placebo crossover protocol. Substantial imrovement with imipramine was demonstrated in adaptive peer interactions, compliance, and bizarre behaviors. This strongly supports consideration of imipramine as part of the intensive inpatient treatment of the borderline syndrome in children. 17 references. (Author abstract modified)

003357 Pickar, D.; Davis, G.; Schulz, C.; Extein, I.; Wagner, R. Unit on Studies of Drug Abuse, Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Behavioral and biological effects of acute beta-endorphin injection in schizophrenic and depressed patients.** American Journal of Psychiatry. 138(2):160-166, 1981.

A dose of beta endorphin (4-15mg) was administered intravenously to six schizophrenic and four depressed patients in a double-blind study. There were neither significant differences in behavioral ratings between these endogenous opioid peptides and placebo for the overall group nor for either schizophrenic or depressed subgroups. Clinical worsening and improvement were observed in individual schizophrenic patients. There was no evidence of late appearing therapeutic effects in four schizophrenic patients rated for 5 consecutive days after placebo and drug infusions. In one patient, 10mg of endorphin produced neuroendocrine effects comparable to that of 5mg i.v. administered methadone. In two other patients, it produced large increases in circulating opioid activity as determined by radioreceptor assay. These biological data support the notion that parenterally administered beta-endorphin exerts significant opiate-like activity in vivo. 56 references. (Author abstract modified)

003358 Pires-de-Oliveira, R. S. Rua 2, 635, 13500 Rio Claro, Brazil **/Action of butriptyline hydrochloride in the gerontopsychiatric patient./** Acao do cloridrato de butriptilina no paciente geronto-psiquiatrico. Jornal Brasileiro de Psiquiatria. 29(2):103-115, 1980.

The action of butriptyline hydrochloride was studied in 50 elderly patients suffering from cerebrovascular insufficiency, who were divided randomly into two groups of 25 Ss each. The first group was administered bencyclane plus butriptyline, while the second group received bencyclane plus placebo. The patients were evaluated subjectively for physical, intellectual, and psychological manifestations and were evaluated objectively with EEGs and the WAIS before and after a period of 60 days' treatment. Results indicate better improvement of the EEG and the WAIS in patients treated with bencyclane plus butriptyline. 19 references. (Journal abstract modified)

003359 Pisani, Francesco D.; Di Perri, Raoul G. Clinica Neurologica dell'Universita, Policlinico G. Martino, I-98013 Contesse, Messina, Italy **Intravenous valproate: effects on plasma and saliva phenytoin levels.** Neurology. 31(4):467-470, 1981.

Plasma and saliva phenytoin was evaluated at fixed time intervals after intravenous administration of 800mg valproate in epileptics chronically treated with phenytoin monotherapy. A significant decrease in plasma and a concurrent significant increase of the drug in saliva (which reflects the free amount in plasma) were observed, with maximal changes occurring at 30 to 90 minutes after valproate infusion. These data indicate that valproic acid is able to diplace phenytoin from plasma proteins, suggesting a critical evaluation of the routine phenytoin plasma levels (which reflect free plus bound fraction) when this drug is administered concurrently with sodium valproate. 19 references. (Author abstract)

003360 Platt, Jane E.; Campbell, Magda; Cohen, Ira L. New York University Medical Center, New York, NY **Effects of lithium carbonate and haloperidol on cognition in aggressive, hospitalized school age children.** Psychopharmacology Bulletin. 17(1):123-125, 1981.

The effects of haloperiodol, lithium, and placebo on the cognitive performance of hospitalized, aggressive schoolage children were assessed as part of a larger study of the therapeutic efficacy of these drug treatments. Children were randomly assigned to one of three treatment groups and were assessed with a series of cognitive tests during the baseline placebo period and after 4 weeks of treatment. Results suggest that for this sample of children, haloperidol has an effect on the ability to maintain a response set. Data indicate that the increased mean reaction time in the haloperidol group reflects a change in attention rather than a general slowing of motor performance. This interpretation is supported by the matching familiar figures task results, in which children on haloperidol responded more quickly on optimal dosage than during baseline testing. A negative effect on Porteus maze qualitative scores was the only cognitive test effect found for lithium. 7 references. (Author abstract modified)

003361 Platt, Jane E.; Campbell, Magda; Green, Wayne H.; Perry, Richard; Cohen, Ira L. Campbell: Dept. of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Effects of lithium carbonate and haloperidol on cognition in aggressive hospitalized school-age children.** Journal of Clinical Psychopharmacology. 1(1):8-13, 1981.

The effects of lithium, haloperidol, and placebo on cognition are reported for a sample of hospitalized school-age children with a behavioral profile of aggressiveness and explosiveness. In this double-blind study, patients were randomly assigned to one of three treatment conditions. The cognitive battery was administered at the end of a 2 week placebo baseline period and again after 4 weeks of treatment. It is included a simple reaction time (RT) task with preparatory intervals of 1, 4, and 8 seconds, the Porteus Mazes, and the Matching Familiar Figures Test. Drug effects on cognitive performance were mild or nonexistent. Slower and more variable RTs were found among the haloperidol group, particularly at the 4 and 8 second preparatory intervals. This effect apparently reflects decreased ability to hold a preparatory set. Lithium caused a deterioration in qualitative performance on the Porteus Maze Test. 43 references. (Author abstract modified)

003362 Polinsky, Ronald J.; Kopin, Irwin J.; Ebert, Michael H.; Weise, Virginia. Laboratory of Clinical Science, NIMH, Bldg 10, Rm 3S-231, 9000 Rockville Pike, Bethesda, MD 20205 **Pharmacologic distinction of different orthostatic hypotension syndromes.** Neurology. 31(1):1-7, 1981.

The pressor responses to vasoactive agents were studied in patients with orthostatic hypotension. Greater than normal slopes of the stimulus response curves inpatients with multiple system atrophy (Shy-Drager syndrome) and idiopathic orthostatic hypotension (IOH) were consistent with deficient reflex modulation. Patients with IOH also had a shift to the left to the plasma norepinephrine blood pressure curves, suggesting denervation supersensitivity. This was consistent with the deficient plasma norepinephrine response to tyramine in these patients. Patients in whom orthostatic hypotension is attended by tachycardia are subsensitive to administered catecholamines, and may suffer from deficient effector organ responsivity. 21 references. (Author abstract)

003363 Porges, Stephen W.; Bohrer, Robert E.; Keren, Gideon; Cheung, Michael N.; Franks, George J.; Drasgow, Fritz. Dept. of Psychology, University of Illinois, Champaign, IL 61820 **The influence of methylphenidate on spontaneous autonomic activity and behavior in children diagnosed as hyperactive.** Psychophysiology. 18(1):42-48, 1981.

The spontaneous autonomic behavior of 13 male and 3 female hyperactive children was examined prior to treatment and following 0.5 or 1mg/kg methylphenidate or placebo. There was a dose related reduction in disruptive classroom behavior and a parallel decrease in a component of heart period variability, V, derived via spectral analysis of heart period activity. The lower dose of methylphenidate, which has been reported to enhance cognitive performance, selectively increased a measure of respiratory/cardiac coupling, Cw, derived via cross-spectral analysis of respiration and heart period activity. It is hypothesized that Cw may be a qunatitative manifestation of brainstem integration and V may be a quantitative estimate of effective vagal tone on the heart. 18 references. (Author abstract modified)

003364 Powers, James S.; Decoskey, Darla; Kahrilas, Peter J. Dept. of Medicine, University Hospitals of Cleveland, Cleveland, OH 44106 **Physostigmine for treatment of delirium tremens.** Journal of Clinical Pharmacology. 21(1):57-60, 1981.

Two patients with complicated delirium tremens were treated successfully with physostigmine. Physostigmine administration resulted in abrupt cessation of the symptoms of delirium tremens and permitted maintenance therapy with low oral doses of benzodiazepines. Results are discussed in relation to the adrenergic/cholinergic imbalance model of delirium tremens. 16 references. (Author abstract modified)

003365 Reid, Andrew H.; Naylor, Graham J.; Kay, David S. G. Strathmartine Hospital, by Dundee DD3 0PG, Scotland **A double-blind, placebo controlled, crossover trial of carbamazepine in overactive, severely mentally handicapped patients.** Psychological Medicine. 11(1):109-113, 1981.

The effect of carbamazepine on 12 severely and profoundly mentally retarded, overactive adult patients was studied in a double-blind, placebo controlled, crossover trial. The trial lasted 7 months and those patients in whom overactivity was the dominant problem responded to some degree to carbamazepine with a reduction in overactivity. This was particularly the case in patients in whom overactivity was accompanied by some elevation of mood. Patients in whom overactivity was part of a wider spectrum of multiple behavior disorders showed a scatter of responses. There was no relationship between response to carbamazepine and the presence or absence of epilepsy. The trial identified a small group of mentally retarded patients in whom carbamazepine might be clinically useful. 9 references. (Author abstract modified)

003366 Reynolds, E. H.; Shorvon, S. D. Dept. of Neurology, Kings College Hospital, Denmark Hill, London S.E. 5, England **Monotherapy or polytherapy for epilepsy?** Epilepsia. 22(1):1-10, 1981.

The utility and clinical efficacy of anticonvulsant polytherapy are reviewed. Polytherapy leads to problems of chronic toxicity, drug interactions, failure to evaluate individual drugs, and sometimes exacerbation of seizures. There are many causes of polytherapy which could be avoided by more careful monitoring and supervision of therapy. Studies in new, previously untreated referrals suggest that there is considerable potential for monotherapy. In the event of failure of optimum monotherapy, there may be scope for careful rationalization to two or sometimes one drug, with reduction in chronic toxicity and sometimes improved seizure control. Reduction of therapy, however, may be impossible or hazardous due to withdrawal seizures. Even after successful reduction, seizure control is much less satisfactory than in new referrals. It is easier to avoid polytherapy than to reduce it. There is a need to define more carefully the limits of effective anticonvulsant therapy. 32 references. (Author abstract modified)

003367 Rodin, Ernst A.; DeSousa, Garcia; Haidukewych, Dan; Lodhi, Rashid; Berchou, Richard C. Epilepsy Center of Michigan, 3800 Woodward, Seventh Floor, Detroit, MI 48201 **Dissociation between free and bound phenytoin levels in presence of valproate sodium.** Archives of Neurology. 38(4):240-242, 1981.

Dissociation between free and bound phenytoin levels in the presence of sodium valproate is reported within the context of a case reported and data from a subsequent study of the relationship between free and bound phenytoin levels in patients receiving the anticonvulsant alone or in combination with other drugs. Findings from previous studies in conjunction with the present data suggest that phenytoin/valproate sodium comedication may lead, at times, to symptoms and signs of phenytoin intoxication, despite plasma levels in the therapeutic range. The importance of supplementing bound level with free level data when combined therapy of this type is used in epileptic patients is emphasized. 14 references. (Author abstract modified)

003368 Saarma, Yu. M.; Saarma, M. M. Tartuskiy universitet, Tartu, USSR **/The role of psychopharmacotherapy in the treatment of elderly patients with organic mental syndromes./** Rol' psikhofarmakoterapii v lechenii bol'nykh pozhilogo vozrasta s organicheskimi psikhicheskimi sindromami. Vestnik Adademii Meditsinskikh Nauk SSSR. No. 12:50-53, 1980.

The role of psychopharmacotherapy in the treatment of elderly patients with organic mental syndromes was studied. A group of 35 patients with moderate atherosclerotic feeblemindedness was treated for 6 weeks with glutamic acid, with a 33% remission rate. Another group of 47 patients with moderate organic mental syndromes was treated for 6 weeks with gamma-aminobutyric acid, with a resulting remission rate of 53%. Results show that the most efficacious drugs for elderly patients with organic mental syndromes are nontropic drugs. Results also show that although psychotropic drugs are important in the combined treatment of elderly patients, they should be used cautiously, and for a clearly formulated purpose, following a thorough examination of the somatic state of the patient, in order to avoid undesirable side-effects which often appear similar to feeblemindedness in elderly patients. 5 references. (Journal abstract modified)

003369 Salzman, Carl. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Psychotropic drug use and polypharmacy in a general hospital.** General Hospital Psychiatry. 3(1):1-9, 1981.

The usage of psychotropic drugs by all general inpatients of a Boston teaching and referral hospital was examined on a randomly chosen weekday. Of all surveyed inpatients, 42.8% were receiving at lease one psychotropic medication. Sleep medications were the most frequently prescribed of all drugs. Phenothiazine and neuroleptics were given to control agitation, pain, or nausea, rather than psychosis. Antidepressants were prescribed without notated justification in the medical record, and if given for depression, were underdosed. Diazepam was the most frequently prescribed psychotropic drug after flurazepam. Psychotropic drug polypharmacy was common with the average patient receiving seven different drugs. Remedial approaches to this widespread problem are recommended. 19 references. (Author abstract)

003370 Serrano, Alberto C. Community Guidance Center, 2135 Babcock Road, San Antonio, TX 78229 **Haloperidol -- its use in children.** Journal of Clinical Psychiatry. 42(4):154-156, 1981.

The use of haloperidol in children is reviewed. Haloperidol has proved to be safe and effective in children for relieving psychotic symptoms associated with childhood autism, schizophrenia, and mental retardation. It is the drug of choice for Tourette's syndrome, and may be useful in nonpsychotic hyperactive or aggressive children to control acute episodes, or when the stimulants normally useful in hyperactive children are ineffective. Such children taking haloperidol not only become calmer, but are often better able to respond to other modalities of therapy and to school instruction. Dosage, initially low is increased gradually to minimize drowsiness and extrapyramidal symptoms, the most common side-effects. It is concluded that haloperidol in children is usually well tolerated. 24 references. (Author abstract)

003371 Shakir, Raad A.; Johnson, Ralph H.; Lambie, David G.; Melville, Ian D.; Nanda, Rabindra N. Johnson: Wellington

Clinical School of Medicine, Wellington Hospital, Wellington 2, New Zealand **Comparison of sodium valproate and phenytoin as single drug treatment in epilepsy.** Epilepsia. 22(1):27-33, 1981.

The effects of sodium valproate and phenytoin as single drug treatment in epilepsy were compared. Thirty three epileptic patients were given sodium valproate or phenytoin for periods ranging from 9 to 48 months (mean, 30 months). Any patient who developed a seizure while on the first drug was changed to the other drug, provided the serum level of the first drug was in the accepted therapeutic range. Six required the change from phenytoin to sodium valproate, and three from sodium valproate to phenytoin. Side-effects were not a major problem with either drug during the trial period. Results indicate that sodium valproate may also be used as a single drug in the treatment of several types of epilepsy. 15 references. (Author abstract modified)

003372 Shapiro, Arthur K.; Shapiro, Elaine. Tourette & Tic Laboratory and Clinic, Mount Sinai School of Medicine, 1 Gustave Levy Place, New York, NY 10029 **The treatment and etiology of tics and Tourette syndrome.** Comprehensive Psychiatry. 22(2):193-205, 1981.

The literature and experience in the treatment of over 800 patients with tics and Tourette syndrome are critically assessed to provide a guide for treatment. Medications are classified and discussed according to their neurochemical actions to provide heuristic insights about the etiology of tics and Tourette syndrome. Major groupings examined include the dopamine antagonists and agonists, the serotonin agonists and antagonists, the cholinergic agonists and antagonists, the antidepressants (tricyclics and monoamine oxidase inhibitors), the anticonvulsants, anxiolytic sedative hypnotic drugs, and others (e.g., baclofen, psychotomimetics, propranolol, clonidine). Miscellaneous therapies used in treatment have included psychotherapy, hypnosis, behavior therapy, the Feingold diet, megavitamins, and various surgical procedures. The effectiveness of haloperidol suggests excessive presynaptic levels of postsynaptic sensitivity or normal levels of dopamine. However, the clinical effects of other drugs with known or presumed actions on neurotransmitters and studies of specific neurotransmitters and their enzymes do not support any of the hypotheses about abnormal levels of dopamine or other catecholamines. Evidence supporting various neuroanatomic or neurochemical theories is inconclusive. 28 references. (Author abstract modified)

003373 Siever, Larry J. National Institute of Mental Health, NIH Clinical Center, 10/3D41, Bethesda, MD 20205 **The effect of amantadine on prolactin levels and galactorrhea on neuroleptic-treated patients.** Journal of Clinical Psychopharmacology. 1(1):2-7, 1981.

The effects of amantadine on prolactin levels and galactorrhea in neuroleptic treated patients were investigated. Amantadine was given to 11 psychotic patients, concurrently on neuroleptic medication, who required treatment of neuroleptic induced extrapyramidal side-effects. Five of the 11 patients suffered from galactorrhea, and all of these reported improvement in their galactorrhea on amantadine. Plasma prolactin levels were measured in 8 of the 11 Ss, and there was a significant decrease in these levels for the group. Presumably these effects are due to amantadine's properties as a dopamine agonist and suggest a possible use of amantadine in the treatment of neuroleptic induced galactorrhea. 55 references. (Author abstract modified)

003374 Singer, H. S.; Rabins, P.; Tune, L. E.; Coyle, J. T. Coyle: Dept. of Pharmacology, Johns Hopkins School of Medicine, 725 North Wolfe Street, Baltimore, MD 21205 **Serum haloperidol levels in Gilles de la Tourette syndrome.** Biological Psychiatry. 16(1):79-84, 1981.

Serum levels of haloperidol were measured in eight Gilles de la Tourette syndrome (GTS) patients, whose dosage had been established by clinical response, and results were compared with those found to be therapeutic in schizophrenia. Results indicated that GTS patients responded to remarkably low oral doses of haloperidol; and serum neuroleptic measurements confirmed the presence of extremely low haloperidol levels, thus ruling out the possibility that patients develop high serum levels despite low doses. In contrast to schizophrenic inpatients, GTS Ss demonstrated marked symptomatic improvement with values on the average tenfold lower than the minimal amount associated with therapeutic response in acute schizophrenic psychosis. These results lend support to the hypothesis of a supersensitive dopaminergic receptor site as the pathophysiologic defect in GTS, and raise the question whether haloperidol may act by a different mechanism in GTS patients than in schizophrenics. 13 references.

003375 So, Elson L.; Penry, J. Kiffin. Dept. of Neurology, Bowman Gray School of Medicine, Winston-Salem, NC 27103 **Epilepsy in adults.** Annals of Neurology. 9(1):3-16, 1981.

A review of advances in the management of the adult epileptic over the past decade is presented. The development of practical long-term EEG techniques, with and without simultaneous video recording, has increased diagnostic accuracy and has provided a method for assessing the clinical efficacy and therapeutic serum concentration of antiepileptic drugs. Computerized tomography has enhanced identification of structural brain lesions. New pharmacotherapeutic concepts have developed from a recognition of the pharmacological properties peculiar to each antiepileptic agent and determination of serum drug levels has been utilized to deal with the problem of intraindividual and interindividual pharmacokinetic variability. A review of the literature on pregnancy in epileptic women reveals that a third to a half experience more seizures during pregnancy; and reduced serum levels of most antiepilepsy drugs have been recently observed during gestation. Although infants of epileptic women taking antiepileptic drugs show a two to threefold increase of risk for infant congenital abnormality, teratogenicity has not yet been demonstrated, with the exception of oxazolidinediones. Modest progress in rehabilitation of epileptics has been made, but serious problems still remain. Several prognostic indicators have been reported, but further research is needed. 184 references. (Author abstract modified)

003376 Sovner, Robert; Hurley, Anne. 300 Mount Auburn St., Suite 410, Cambridge, MA 02238 **The management of chronic behavior disorders in mentally retarded adults with lithium carbonate.** Journal of Nervous and Mental Disease. 169(3):191-195, 1981.

The medical literature is reviewed and two case histories are presented regarding the efficacy of lithium carbonate in treating chronic behavior disorders in mentally retarded adults. Available data tentatively support the use of lithium to manage such disorders when they are characterized by life long hyperactivity, aggressiveness, and/or self-mutilation. When lithium is used for this indication, a blood level of approximately 1.0mEq/l is considered necessary, and all patients should be given a drug free trial once a therapeutic effect has been achieved in order to assess the continued need for treatment. Etiological issues, a possible mechanism of action involving lithium's effect on CNS serotonergic activity, and areas for future research are discussed. 22 references. (Author abstract modified)

003377 Summers, William K.; Viesselman, John O.; Marsh, Gary M.; Candelora, Kent. University of Southern California, Los Angeles, CA 90007 **Use of THA in treatment of Alzheimer-**

like dementia: pilot study in twelve patients. Biological Psychiatry. 16(2):145-153, 1981.

THA (1,2,3,4 tetra-hydro-5-aminoacridine), a centrally acting anticholinesterase, was tested in varying intravenous doses with 12 unselected cases of Alzheimer-like senile dementia. Significant improvement in memory testing occurred in six Ss; nine Ss improved in clinical staging. Analysis of results with respect to staging of dementia revealed that the degree of improvement was inversely related to the severity of dementia. Statistical analysis of these data by the Friedman test is detailed. 21 references. (Author abstract)

003378 Sutula. Thomas P.; Sackellares, J. Chris; Miller, James Q.; Dreifuss, F. E. Dreifuss: Dept. of Neurology, University of Virginia School of Medicine, Charlottesville, VA 22908 **Intensive monitoring in refractory epilepsy.** Neurology. 31(3):243-247, 1981.

Forty patients with intractable seizures were studied in an epilepsy unit for an average of 8 weeks with video EEG telemetry and continuous observation by trained personnel. Drugs were administered on the basis of antiepileptic drug measurements and seizure classification determined by clinical observation and telemetry. Seizure frequency was reduced in 24 patients (60%). Unrecognized seizure types were identified in eight patients (20%), and diagnostic classification was changed in 19 patients (47.5%). At least one antiepileptic drug was eliminated in 25 patients (60%), and the average drug reduction per patient was significant. In patients with seizures refractory to conventional outpatient and hospital management, improvement in diagnostic accuracy and refinement in observation techniques result in significant reduction of seizure frequency, elimination of drugs, and limitation of toxicity. 14 references. (Author abstract modified)

003379 Toro-G., Ricardo Jose; Holguin-A., Jorge. Universidad de Antioquia, Medellin, Colombia **/Gilles de la Tourette syndrome./** Enfermedad de Gilles de la Tourette. Revista Colombiana de Psiquiatria. 8(2):146-157, 1979.

The symptomatology and treatment of patients with Gilles de la Tourette syndrome were studied. A sample of six children with the disease were interviewed and examined thoroughly. The children presented tics, vocalizations, coprolalia, and sexual impulses. Two children demonstrated abnormal EEG patterns, and one child showed epileptic symptoms. The children were treated with haloperidol, which appeared to improve the symptoms. It is recommended that low doses of haloperidol be continued and then gradually increased. 13 references.

003380 Tu, Jun-bi. Penrose Division, Ongwanada Hospital, 752 King Street, Kingston, Ontario, Canada K7L 4X3 **Phenylketonuria: the inadvisability of neuroleptic medication.** Biological Psychiatry. 15(5):797-802, 1980.

The use of neuroleptic medications in two disturbed phenylketonuria patients was studied over a period between 4 and 5 years. The outcome of clinical observation, supported by the neurochemical findings, suggests that most neuroleptic medications may be less than indicated for treating these patients. The observation provides an important example of how an adverse neuroleptic drug response can be predicted by baseline biochemical measures which are closer to the basic pathophysiology of the condition and the site of psychotropic drug action. 19 references. (Author abstract)

003381 Umstead, Greg S.; McKernan, Thomas. College of Pharmacy and Allied Health Professions, Wayne State University, Detroit, MI 48202 **Phenytoin concentrations in venous versus capillary blood of geriatric patients.** Journal of the American Geriatrics Society. 29(1):34-36, 1981.

In 15 elderly patients who had seizure disorders, venous blood (standard venipuncture) was compared with capillary blood (finger lancet puncture) as the source of the specimen for determination of serum phenytoin concentration. All patients at the time of collection were taking an oral phenytoin preparation for control of seizures. The values obtained by the two procedures were similar. The mean serum phenytoin levels in the venous samples was 17.3mcg/ml, and in the capillary samples 17.0mcg/ml; the paired t test showed no statistical difference. It is concluded that either method provides an adequate blood sample for determination of phenytoin, and both may be used interchangeably. Capillary samples may be preferable for aged patients in whom venipuncture proves difficult or painful. 19 references. (Author abstract)

003382 Villa, D.; Armocida, G.; Mayeron, M. A. Ospedale Neuropsichiatrico Provinciale, Varese, Italy **/Intracellular lithium: its value in the prediction of a positive response to lithium./** La litiemia intracellulare: suo valore nel predire una risposta positiva al litio. Minerva Psichiatrica. 21(1):49-54, 1980.

Cellular lithium values are discussed with reference to an original study. The red cell lithium/plasma ratio is a variable associated with the positive response to treatment with lithium carbonate. Lithium/plasma ratio levels are high in persons with positive responses and low in nonresponders. These findings in the literature are confirmed by a study conducted at a psychiatric hospital with nine responders and eight nonresponders. The marked difference in ratio values is consistent with the correlation demonstrated between this parameter and the efficacy of the response to treatment with lithium carbonate. 35 references. (Journal abstract modified)

003383 Volavka, Jan; Simeon, Jovan; Simeon, Susan; Cho, Dong; Reker, Dean. Manhattan Psychiatric Center, Ward's Island, NY 10035 **Effect of piracetam on EEG spectra of boys with learning disorders.** Psychopharmacology. 72(2):185-188, 1981.

Piracetam was compared with placebo in a double-blind, crossover study of 30 learning disabled boys. Power spectral analyses revealed that piracetam caused a decrease in the amount of delta activity and an increase in the average EEG frequency. This result is in agreement with findings obtained by other workers in adult patients. It is suggested that some clinical effects of piracetam may be mediated by increased alertness and/or decreased fatigue. 11 references. (Author abstract modified)

003384 Vovin, R. Ya.; Gurevich, Z. P.; Skorik, A. I.; Zatonskaya, M. S.; Kyunnapu, I. V. Otd. klinicheskoy psikhofarmakologii Leningradskogo nauchno-issled. psikhonevrologicheskogo inst. im. V. M. Bekhtereva, Leningrad, USSR **/On the intensive treatment of endogenous psychoses./** Ob intensivnoy terapii endogennykh psikhozov. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(6):909-914, 1980.

An experiment to determine the effects of various treatment methods on patients suffering from severe endogenous psychoses was conducted using 170 subjects, of whom 100 were treated with intensive methods and 70 with traditional methods. It was found that a reduction in hospitalization time was possible in the case of those given the intensive treatment, which included intravenous drip administration of drugs with rapidly increasing dosage, rapid neuroleptization, and combinations of psychotropic drugs with other biological treatment. It is concluded that such intensive therapy is desirable only in acute psychoses and only during their early stages. 19 references. (Journal abstract modified)

003385 Vroulis, George A.; Smith, Robert C.; Brinkman, Samuel; Schoolar, Joseph; Gordon, Jack. Section of Biological Psychiatry, Texas Research Institute of Mental Sciences, Medical Center, Houston, TX **The effects of lecithin on memory in patients with senile dementia of the Alzheimer's type.** Psychopharmacology Bulletin. 17(1):127-128, 1981.

The effects of lecithin on memory and learning were studied in 18 patients with symptoms consistent with senile dementia of the Alzheimer type (SDAT). Preliminary results indicate that nine out of 15 patient improved in the total recall subscale of the Buschke Selective Reminding (BSR) procedure, with six out of 15, eight out of 15, and 10 out of 15 improving on the short-term recall, long-term recall, and long-term storge subscales of the BSR, respectively. Lecithin treatment also significantly reduced two cholesterol risk ratios: total cholesterol per high density lipoprotein and total cholesterol per low density lipoprotein. These lipid ratios have been shown to be correlated with the development of atherosclerosis. 12 references. (Author abstract modified)

003386 Walker, Mary Klotz. University of Illinois at the Medical Center **Effects of methylphenidate hydrochloride on repeated acquisition behavior in hyperkinetic children. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2561-B, 1981. Ann Arbor, Univ. Microfilms No. 8021326, 123p., 1980.

The effects of two therapeutic doses or orally administered methylphenidate hydrochloride or placebo on the learning behavior maintained by a repeated acquisition task in hyperkinetic children were examined with 18 children aged 6 to 12.5 years. Two hours after drug administration the Ss performed two repeated acquisition sequences. Each child was reinforced for the successful completion of the appropriate response requirement irrespective of the amount of time to successful completion. The primary treatment effects on the dependent variable, mean error, are attributable to the error decreasing effect of the methylphenidate hydrochloride. The repeated acquisition task constitutes an efficient method of investigating the effects of therapeutic doses of stimulant drugs on learning behavior in hyperkinetic children by maintaining a behavior which is sensitive to drug effect within the narrow range commonly administered to children. (Journal abstract modified)

003387 Walter, L. Kinderneuropsychiatrische Poliklinikum Abteilung, Betriebskrankenhaus, Poliklinikum, Hoyerswerda, West Germany **/On the evaluation of a provocative EEG method using medication in the diagnosis of organic brain seizures in childhood, with special emphasis on sleep induction through medication./** Zur Einschatzung medikamentoser Provokationsmethoden des EEG bei der Diagnostik hirnorganischer Anfallsleiden im Kindesalter unter besonderer Berucksichtigung der medikamentosen Schlafinduktion. Zeitschrift fur Arztliche Fortbildung. 73:257-262, 1979.

Sleep induction by the tranquilizer Sinophenin promazine was investigated using the EEG in a study of 145 children and adolescents ranging up to age 16. Different dosages of the drug were administered according to age and weight. The correlation between the obtained clinical and bioelectrical diagnoses was considered in relation to ontogenetic brain development. The relation of the particular type of organic brain seizure to S's age, the wake and sleep rhythms, and the pharmacological changes causing modification of this rhythm are discussed. (Journal abstract modified)

003388 Weingartner, Herbert; Gold, Philip; Ballenger, James; Smallberg, Sheila; Summers, Richard; Rubinow, David; Post, Robert; Goodwin, Frederick NIMH, Bethesda, MD 20205 **Effects of vasopressin on human memory functions.** Science. 211(4482):601-603, 1981.

The effects of arginine vasopressin on human memory functions were investigated. One of its synthetic analogs, 1-desamino-8-D-arginine vasopressin (DDAVP) was administered for a period of several days to cognitively unimpaired as well as cognitively impaired adults. Both groups learned information more effectively as measured by the completeness, organization, and consistency (reliability) of recall. DDAVP also appeared to reverse partially the retrograde amnesia that follows electroconvulsive treatment. 15 references. (Author abstract)

003389 Wender, Paul H.; Reimherr, Frederick W.; Wood, David R. Dept. of Psychiatry, University of Utah, 50 N. Medical Dr., Salt Lake City, UT 84132 **Attention deficit disorder ('minimal brain dysfunction') in adults: a replication study of diagnosis and drug treatment.** Archives of General Psychiatry. 38(4):449-456, 1981.

An attempt was made to replicate an earlier study dealing with the diagnosis and treatment of attention deficit disorder (ADD or minimal brain dysfunction) in adults. Subjects who met provisional operational criteria for adult ADD were entered in a random assignment, parallel, double-blind trial of placebo and pemoline, a noneuphorigenic psychostimulant drug effective in children with ADD. There was improvement in both the pemoline group and the placebo group, but the difference in improvement was not statistically significant. When the analyses were confined to that subgroup of patients whose parents had described them in the 95th percentile of childhood hyperactivity or when the hyperactivity score was partialled out statistically, pemoline was demonstrably more effective than placebo. Revised operational criteria for adult ADD are proposed. 55 references. (Author abstract modified)

003390 Wenzel, Ulf. Landshuter Strasse 65, D-8400 Regensburg, West Germany **/Lithium treatment of the Kleine-Levin syndrome./** Therapie mit Lithium beim Kleine-Levin-Syndrom. Zeitschrift fur Kinder- und Jugendpsychiatrie. 7(3):219-220, 1979.

The usefulness of lithium in juvenile insomnia, and especially in the Kleine-Levin syndrome, is discussed in the light of recent findings that recurrence of hypersomniac episodes is potentially preventable in adolescents by administering lithium carbonate. Long-term controlled treatment with lithium promises to be effective in the prophylaxis of the Kleine-Levin syndrome. In cyclothymic psychoses, however, the prophylactic effects of lithium are limited on account of slow absorption. 2 references. (Journal abstract modified)

003391 Wittenborn, J. R. Interdisciplinary Research Center, Rutgers University, New Brunswick, NJ 08903 **Pharmacotherapy for age-related behavioral deficiencies.** Journal of Nervous and Mental Disease. 169(3):139-156, 1981.

A distinction is made between drugs for treating age related behavioral losses or impairments among the elderly (Ss age 65 and older) and the psychopharmacotherapeutic drugs used in treating disturbed or disordered behavior in adults of various ages. Placebo controlled studies confirm numerous responses to drugs designed specifically for treating impaired behavior in the aged, and the responses of normal or mildly impaired Ss to some of these drugs suggest the possibility of prophylactic applications. The various drug classes include compounds affecting circulatory and metabolic activity and familiar psychotropic medications (major and minor tranquilizers, stimulants, and antidepressants). 156 references. (Author abstract modified)

003392 Wysocki, Tim; Fuqua, Wayne; Davis, Vicky J.; Breuning, Stephen E. Fuqua: Dept. of Psychology, Western Michigan University, Kalamazoo, MI 49008 **Effects of thioridazine (Mellaril) on titrating delayed matching-to-sample performance of mentally retarded adults.** American Journal of Mental Deficiency. 85(5):539-547, 1981.

The effects of thioridazine on the performance of a titrating delayed matching to sample discrimination by four retarded adults were examined. The delay between depression of a center response panel and presentation of two comparison stimuli on the side response panels varied according to the accuracy of the Ss' performance. The primary dependent variable was the limit of delay, defined as the longest delay at which the Ss emitted four consecutive correct responses in a 30 minute session. The Ss chronic doses of thioridazine were reduced systematically in a multiple baseline across subjects design. For all Ss, the limit of delay increased only after reductions in the daily thioridazine dose had been implemented. Results indicate that the withdawal of chronically administered thioridazine results in increased accuracy in a delayed matching to sample task. Findings suggest that the drug repairs performance of this discrimination. 28 references. (Author abstract modified)

003393 Yesavage, Jerome A.; Westphal, James; Rush, Leonard. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Palo Alto, CA 94305 **Senile dementia: combined pharmacologic and psychologic treatment.** Journal of the American Geriatrics Society. 24(4):164-171, 1981.

Either supportive counseling (SC) or cognitive training (CT) was used to enhance the efficiency of a standard pharmacologic treatment for dementia, dihydroergotoxine mesylate (DEM). DEM was administered orally to 21 moderately demented subjects, in a dosage of 1mg three times daily; and SC or CT was conducted for 1 hour every 2 weeks for a total of 12 weeks. The CT was designed to enhance memory and other intellectual functions by the teaching of organizational schemes and mnemonic devices. The DEM plus CT group of patients improved more than did the DEM plus SC group for the measures of memory and learning. However, no differences are noted between groups for the Hamilton Rating Scale for Depression or Sandoz Clinical Assessment-Geriatric behavioral measures. 44 references. (Author abstract modified)

003394 Yudofsky, Stuart; Williams, Daniel; Gorman, Jack. Dept. of Psychiatry, Columbia University College of Physicians and Surgeons, 722 West 168th St., New York, NY 10032 **Propranolol in the treatment of rage and violent behavior in patients with chronic brain syndromes.** American Journal of Psychiatry. 138(2):218-220, 1981.

The successful treatment of four patients with irreversible CNS lesions and socially disabling aggressiveness and outbursts of rage is reported. The patients' behavior, which had not been affected by high doses of major tranquilizers or anticonvulsants, were treated with 320-520mg/day of propranolol. Disorientation, memory impairment, and psychotic thought processes associated with the CNS lesions were not altered by the drug. 7 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

003395 Jacobs, Rosevelt, Nowell, Maxine. Dept. of Psychiatry, Charles R. Drew Postgraduate Medical School, 12021 S. Wilmington Avenue, Los Angeles, CA 90059 **Phencyclidine hydrochloride: a challenge to medicine.** Journal of the National Medical Association. 73(2):170-172, 1981.

An overview of phencyclidine hydrochloride (PCP) abuse and its management is presented. PCP first became available as a street drug in 1967 and is one of the most dangerous of the drugs of abuse. Its use is most prevalent among adolescents and young adults. In subanesthetic doses, PCP's effects proceed in three stages: changes in body image, sometimes accompanied by depersonalization; perceptual distortions and visual or auditory hallucinations; and feelings of apathy and suicidal ideation. Many users have reacted with acute psychotic episodes; because of the often bizarre and dangerous behavior, PCP abuse has an enormous impact upon the abuser's family. PCP psychosis, accompanied by paranoia, hostility, unpredictability, and a tendency toward violence constitutues a psychiatric emergency. Treatment requires prompt hospitalization, haloperidol, and group psychotherapy after the acute phase has passed. Because of the hazards associated with PCP abuse, the need for public education is emphasized. 7 references.

003396 Schultzes, Richard E.; Hoffmann, Albert. no address / **The world of hallucinogenic plants.**/ Plants of the Gods. London, Hutchinson, 1980. L12.95.

Following a discussion of the meaning of terms such as hallucinogenic, narcotic, and psychotomimetic, a review of the plant kingdom is presented focusing on the presence or absence of hallucinogens in each group of plants and their geographic distribution. The manner in which the hallucinogenic principles have been isolated is described, and a plant lexicon is presented which reviews the botanical and other properties of the 91 principle hallucinogenic plants. Use of hallucinogenic plants among aboriginal and primitive peoples for magical, religious, and medical purposes is then considered. Finally, the chemical structure of the hallucinogens and their use in modern medicine is examined. Illustrations are provided.

003397 Yamamoto, Tsuneyuki; Ueki, Showa. Dept. of Pharmacology, Kyushu University, Maidashi 3-1-1, Higashi-ku, Fukuoka 812, Japan **The role of central serotonergic mechanisms on head-twitch and backward locomotion induced by hallucinogenic drugs.** Pharmacology Biochemistry and Behavior. 14(1):89-95, 1981.

Head twitch induced in female Wistar King-A rats by lysergic acid diethylamide, mescaline, or 2,5-dimethoxy-4-methylamphetamine (DOM) was significantly increased by medial raphe (m-R) lesions, but not by dorsal raphe (d-R) lesions. Hallucinogen induced head twitch was inhibited by methysergide and increased by p-chlorophenylalanine (PCPA). Backward locomotion induced by DOM was reversed by m-R lesions, combined m-R and d-R lesions, or methysergide, but not by d-R lesions or PCPA. 28 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

003398 Andreyeva, O. G.; Meyerson, Ya. A.; Shchelkunov, Ye. L. Psikhonevrologicheskiy institut im. V. M. Bekhtereva, Leningrad, USSR /**The stimulating effect of amphetamine on the visual system.**/ Stimuliruyushcheye vliyaniye fenamina na zritel'nuyu sistemu. Fiziologiya Cheloveka. 6(3):440-446, 1980.

The stimulating effect of amphetamine on the visual system was studied with the aid of a two channel electronic optical tachistoscope. Results show that: 1) amphetamine in a 15 to 20mg dose (.024 to 0.29mg/kg) exerts a stimulating effect on the human visual system according to the criterion of liminal recognition time of visual images; 2) pimozide in a 4mg dose (0.05 to 0.08mg/kg) does not exert a depressant influence on visual functioning; 3) pimozide blocks the stimulating effect of amphetamine on the visual system; and 4) the dihydroxyphenylalanine aminergic component of the action of amphetamine may play a leading role in stimulating the human visual system. 31 references.

003399 Aronson, Jeffrey K.; Grahame-Smith, David G. MRC Unit and University Dept. of Clinical Pharmacology, Radcliffe Infirmary, Oxford, England OX2 6HE **Clinical pharmacology: adverse drug interactions.** British Medical Journal. No. 6260:288-291, 1981.

The incidence and mechanisms of adverse drug interactions are examined, and examples of clinically important interactions are cited. In general, when two drugs interact one precipitates the interaction while the other is the object of the interaction. Three types of drug interactions are pharmaceutical, pharmacokinetic, and pharmacodynamic. Pharmaceutical interactions are those of a drug either with another drug in the same infusion solution or with the infusion solution itself. Ways to avoid such interactions are noted. Pharmacokinetic interactions are those interactions in which the disposition of the object drug is altered in some way by the precipitant drug. These interactions can be considered according to the altering of absorption, protein binding, metabolism, active transport, or excretion. Pharmacodynamic interactions may be either direct or indirect. The most common direct pharmacodynamic interactions are those resulting from drugs acting on the central nervous system. Sources of information about drugs interactions are listed. 9 references.

003400 Barber, H. E.; Petrie, J. C. Dept. of Pharmacology, University of Aberdeen, Aberdeen AB9 2ZD, Scotland **Clinical pharmacology: elimination of drugs.** British Medical Journal. No. 6266:809-810, 1981.

The principles of drug elimination, primarily by the liver and kidneys, are outlined. Most elimination processes of drugs follow first-order elimination kinetics. In such processes, a defined and constant fraction of the drug is irreversibly eliminated in a constant time. The half-life time in such first-order processes is the time taken for the drug concentration to fall to half its original value. Some drugs, such as ethyl alcohol, follow zero-order elimination kinetics. In these processes, elimination occurs at a constant rate because the enzymes necessary for drug metabolism and the active excretion processes become saturated. Factors affecting drug clearance include the lipid solubility of the drug, the rate of delivery of the drug to the organs of elimination, and the capacity of the organs of elimination. 6 references. (Author abstract modified)

003401 Barkin, R. M.; Weston, W. L.; Humbert, J. R.; Maire, F. Dept. of Pediatrics, University of Colorado Health Sciences Center, 4200 East Ninth Ave., Denver, CO 80262 **Phagocytic function in Down syndrome -- I. Chemotaxis.** Journal of Mental Deficiency Research. 24(4):243-249, 1980.

The influence of trisomy 21 on phagocytic function was investigated in 14 Down syndrome and 15 matched institutionalized controls, and a nonmatched comparison normal group representing noninstitutionalized young adults. Neutrophil chemotaxis in both institutionalized groups was significantly impaired. Monocyte chemotaxis was also lower than that of normal Ss. Evaluation of humoral components of neutrophil chemotaxis revealed no significant differences between the two institutionalized groups. Down syndrome Ss had diminished monocyte chemotactic responses compared with the other two groups. The results have implications for studies of the increased incidence of bacterial and viral infections in Down syndrome individuals and in other chromosomal abnormalities. 26 references. (Author abstract modified)

003402 Brown, Gregory M.; Grof, Eva; Grof, Paul. Dept. of Neurosciences and Psychiatry, McMaster University, Hamilton, Ontario Canada **Neuroendocrinology of depression -- a discussion.** Psychopharmacology Bulletin. 17(1):10-12, 1981.

The effects of lithium chloride administration on neuroendocrine function in normal volunteers were investigated, and selected studies of the neuroendocrinology of depression are reviewed. Three volunteers received lithium for 3 weeks, and growth hormone, luteinizing hormone, and prolactin response to insulin hypoglycemia and to combined thyroid releasing hormone and luteinizing hormone releasing hormone were examined. Lithium treatment resulted in a pronounced attenuation, both in the growth hormone response to insulin hypoglucemia and also in the prolactin response to hypoglycemia. This highly specific effect on the hypolglycemia response cannot be explained through an effect on dopamine systems, as dopamine mechanisms exert opposing effects on growth hormone and prolactin. Methodological implications are noted. 12 references. (Author abstract modified)

003403 Caille, Emile-Jean. Centre d'Etude et de Recherche de Psychologie Appliquee, F-83800 Toulon, France **/Study of the effects of PC-63-14 on the quantified EEG./** Etude des effects due PC 63-14 sur l'E.E.G. quantifie. Psychologie Medicale. 12(10):2237-2246, 1980.

Th effects of PC-63-14 (potassium salt of acetylaminosuccinic acid) on the quantified EEG were studied. A double-blind crossover comparison of PC-63-14 and placebo was undertaken under normal atmospheric conditions in 12 volunteer subjects, 6 of whom were diagnosed as being anxious. The drug or placebo was administered for 14 days, and each study period was separated by a 7 day washout period. Spectral analysis of the EEG tracing shows that PC-63-14 exerted a psychoanaleptic effect on the right hemisphere and facilitated interhemispheric coordination. 5 references. (Journal abstract modified)

003404 Caridroit, Marguerite; Tauziede-Castel, Catherine; Caridroit, Michel; Fontan, Michel. Lab. de la Chaire d'Hydrologie therapeutique et climatologie, Cedex U.E.R. de medecine, 1, place de Verdun, F-59045 Lille Cedex, France **/Abnormal transmethylation reaction during the metabolism of dopamine, tryptamine, and serotonin, and schizophrenic symptoms: a critical review./** Reaction de transmethylation anormale de la dopamine, de la tryptamine et de la serotonine et symptomes schizophreniques: revue critique. Psychologie Medicale. 12(11):2405-2420, 1980.

Transmethylation during the metabolism of dopamine and serotonin in schizophrenics is examined. Certain similarities exist between some schizophrenic symptoms and psychic disturbances induced by psychodysleptic drugs, and structural similarities were found between these drugs and chemical mediators. Characteristics of abnormal transmethylation are: concentration of S-adenosyl-L-methionine, enzyme activity of methoxylation and of N-methyl-transferase, excess of 5-methyltetrahydrohomo folic acid, and enzyme activity of MAO. The three amines which were found to be connected to this problem are: 4-methylenedioxyamphetamine, 3,4-dimethoxyphenethydamine, and 6-hydroxydopamine. 101 references. (Journal abstract modified)

003405 Diamond, Eric L.; Carver, Charles S. Dept. of Psychology, PO Box 248185, University of Miami, Coral Gables, FL 33124 **Sensory processing, cardiovascular reactivity, and the type A coronary-prone behavior pattern.** Biological Psychology. 10(4):265-275, 1980.

An investigation was conducted of the hypothesis that the two modes of sensory processing known to elicit integrated patterns of cardiovascular reactivity will arouse exaggerated responses in type-A coronary prone individuals. Fifteen (15) type-A and 10 type-B male college students performed on two tasks calling for sensory intake and sensory rejection, respectively, while being monitored for heartrate, blood pressure, and vasomotor response. Contrary to prediction, the tasks failed to differentiate the groups, although each task appeared to elicit the expected pattern of cardiovascular response across groups. It is suggested that sensory processing tasks per se may be insufficiently challenging to elicit the characteristic hyperresponsivity of the type-A. 34 references. (Author abstract)

003406 Eisler, Toomas; Eng, Nancy; Plotkin, Charles; Calne, Donald B. Calne: Experimental Therapeutics Branch, NINCDS, NIH, Bethesda, MD 20205 **Absorption of levodopa after rectal administration.** Neurology. 31(2):215-217, 1981.

Absorption of levodopa was studied in 12 parkinsonian patients after administration by mouth and rectum. Given by mouth, levodopa benefited all 12 patients studied, and levodopa blood levels rose significantly. When it was given rectally, there was no rise in levodopa concentration in the blood and no clinical benefit. Rectally administered levodopa is therefore of no value in the management of postoperative parkinsonian patients who cannot take oral medication. 13 references. (Author abstract modified)

003407 Friedhoff, Arnold J.; Miller, Jeannette C. Dept. of Psychiatry, New York University School of Medicine, New York, NY **Nongenetic factors affecting human platelet monoamine oxidase.** Psychopharmacology Bulletin. 17(1):101-103, 1981.

Research studies of nongenetic factors affecting human platelet monoamine oxidase (MAO) are reviewed. It is noted that MAO activity as measured in the usual assay in platelets, can be considered to be a function of at least four major factors: 1) the status of the MAO gene; 2) nongenetic factors affecting the MAO enzyme protein; 3) factors affecting the assay; and 4) nongenetic factors affecting the platelet, and thereby secondarily altering the apparent MAO activity. Studies concerning the influence of neuroleptic regimens on MAO levels in schizophrenic patients are cited. 12 references. (Author abstract modified)

003408 Garcia-Sevilla, Jesus A.; Zis, Athanasios P.; Zelnik, Thomas C.; Smith, Charles B. Smith: Dept. of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109 **Tricyclic antidepressant drug treatment decreases alpha2-adrenoreceptors on human platelet membranes.** European Journal of Pharmacology. 69(1):121-123, 1981.

Chronic administration of imipramine to psychiatric patients led to a significant decrease (35%) in the number of high affinity binding sites for 3H-clonidine on their blood platelet membranes. The number of alpha2-receptor binding sites was also reduced on platelets from a depressed patient treated with nortriptyline (75mg/day for 5 weeks). Binding parameters in drug free patients did not differ from those in a normal control population. Tricyclic antidepressant drugs also inhibited the binding of 3H-clonidine to platelet membranes in vitro, but this inhibition was competitive and not associated with a change in the number of binding sites. Results suggest that the specific binding of radiolabelled alpha2-receptor ligands to human platelet membranes may be a useful test of therapeutic responsiveness in endogenous depression and other clinical disorders that involve altered noradrenergic function. 5 references.

003409 Gorman, Jack M.; Fyer, Abby F.; Gliklich, Jerry; King, Donald; Klein, Donald F. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Effect of sodium lactate on patients with panic disorder and mitral valve prolapse.** American Journal of Psychiatry. 138(2):247-249, 1981.

A group of 16 panic disorder patients with mitral valve prolapse were studied to determine if they were also sensitive to sodium lactate and, if so, whether the infusion test response would distinguish them from patients without prolapsed mitral valve. The presence or absence of such a valve had no influence on induction of a panic attack by sodium lactate, and the evidence suggests that panic disorder is a single entity. Further research is recommended to study the types of other types of stress attacks in patients with anxiety neurosis. 10 references.

003410 Greenblatt, David J. Div. of Clinical Pharmacology, Box 1007, New England Medical Center Hospital, 171 Harrison Ave., Boston, MA 02111 **Clinical pharmacokinetics of oxazepam and lorazepam.** Clinical Pharmacokinetics. 6(2):89-105, 1981.

The clinical pharmacokinetics of oxazepam and lorazepam, 3-hydroxy benzodiazepine derivatives used as sedatives and anxiolytics, are reviewed. The major metabolic pathway for both compounds involves conjugation to glucuronic acid at the 3-position, followed by urinary excretion of the inactive glucuronide metabolite. Oxazepam has been administered to humans by the oral route only. Usual ranges for kinetic parameters are: elimination half-life, 5 to 15 hours; volume by distribution, .6 to 2L/kg; and clearance, .9 to 2ml/min/kg. Age and liver disease have a minimal influence on oxazepam kinetics, but renal disease is associated with prolonged half-life and increased volume of distribution. Typical kinetic values for lorazepam are: elimination half-life, 8 to 25 hours; volume of distribution, 1 to 1.3L/kg; and clearance, .7 to 1.2ml/min/kg. Lorazepam clearance is somewhat reduced in old age, but liver disease has a minimal effect on clearance. Oral and intramuscular lorazepam are rapidly absorbed, with systemic availability averaging 90% or more. Both drugs are extensively bound to plasma protein, but the free fraction for lorazepam (8% to 12%) is greater than that for oxazepam (2% to 4%). 59 references. (Author abstract modified)

003411 Halbreich, Uriel; Asnis, Gregory M.; Halpern, Frieda; Tabrizi, Mary Ann; Sachar, Edward J. Montefiore Hospital and Medical Center, 111 East 210th St., Bronx, NY 10467 **Diurnal growth hormone responses to dextroamphetamine in normal young men and postmenopausal women.** Psychoneuroendocrinology. 5(4):339-344, 1980.

In normal postmenopausal women, growth hormone (GH) response to dextroamphetamine was found to be small and significantly less than that seen in young normal men. In postmenopausal women, but not in young men, the GH response to amphetamine was significantly higher in the evening than in the morning. The reduced GH responses to dextroamphetamine in postmenopausal women may be due to sex difference, hypoestrogenism, or to reduced brain catecholamines associated with age. The diurnal variation of the GH response to d-amphetamine in postmenopausal women may reflect a diurnal variation in hypothalamic noradrenergic activity which was not masked by a reciprocal variation in estradiol levels. 24 references. (Author abstract modified)

003412 Herrmann, W. M.; Hofmann, W.; Kubicki, St. Institut fur Arzneimittel des BGA, Postfach 330013, D-1000 Berlin 33, West Germany **Psychotropic drug induced changes in auditory averaged evoked potentials: results of a double-blind trial using an objective fully automated AEP analysis method.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 19(2):56-62, 1981.

An automated procedure was used to study the effects of single oral doses of diazepam (10mg), dextroamphetamine (20mg), amitriptyline (75mg), haloperidol (3mg), and placebo on the auditory averaged evoked potential (AEP) in 15 healthy male volunteers. Diazepam and amytriptyline increased the latency for early components and decreased latency for late components. Dextroamphetamine decreased the latency of early components and increased the latency of late components. Amitriptyline and diazepam produced an area shift from the early to late AEP. Dextroamphetamine did not influence the AEP distribution, but produced a general decrease in amplitude, as did diazepam. Haloperidol had only slight effects on the AEP. Component P3 was decreased by dextroamphetamine and placebo, but increased by diazepam, amitriptyline, and haloperidol. 19 references. (Author abstract modified)

003413 Itil, Turan M.; Schneider, Sid J.; Fredrickson, John W. Division of Biological Psychiatry, Dept. of Psychiatry, New York Medical College, Valhalla, NY **The replicability of the psychophysiological effects of diazepam.** Biological Psychiatry. 16(1):65-70, 1981.

The replicability of the psychophysiological effects (central and peripheral) of diazepam was examined in seven healthy, White male Ss. Ss reported for 12 sessions with at least 48 hr between sessions; Ss received either placebo or 10mg diazepam and computerized EEG (CEEG) and electrodermal readings were obtained 1 and 3 hr later. In each of the 10 diazepam sessions, diazepam induced increased in frequencies below 7.5 cycle/sec and above 20 cycle/sec and decreases in alpha (7.5 to 13 cycle/sec) activity in the primary wave, and increases between 20 and 40 cycle/sex in the first derivative. When each of the CEEG profiles were classified based on the HZI Data Base of Psychotropic Drugs, the response in every session was classified as anxiolytic. Electrodermal data yield a similar picture; diazepam generally lowered skin conductance level, and to a greater extent than placebo. Results replicate previous findings and indicate that these results are replicable across repeated measures. 11 references.

003414 James, Angela L.; Barry, Robert J. Barry: School of Education, University of New South Wales, Kensington 2033, Australia **Habituation of electrodermal and respiratory responses to visual stimuli as a function of personality differences in affect level.** Biological Psychology. 10(4):253-264, 1980.

The relationship between personality level of affect and habituation of electrodermal and respiratory measures was examined in two groups of normal Ss designated low P (LP) and high P (HP) according to the psychoticism (P) scale of the Eysenck Personality Questionnaire. Experiment 1 examines changes as a function of repeated presentation of simple visual stimuli. Group HP displayed reduced habituation rates for both respiratory pause and skin resistance response, although initial reactivity levels were similar for both groups. This effect was confirmed more strongly in Experiment 2, which utilized a simple counting task and groups more widely separated on P. The implications of these group differences are discussed in relation to the psychophysiological functioning of autistic children. 23 references. (Author abstract)

003415 Kawahara, Ryuzo; Hazama, Hidebumi; Fukuhara, Tomokazu; Takeshita, Hisayoshi; Tamura, Tatsuyoshi. Dept. of Neuro-psychiatry, Tottori University School of Medicine, Yonago 683, Japan **Biological effects of chlorpromazine in chronic schizophrenics. I. With reference to pituitary hormones.** Kyushu Neuro-Psychiatry. 26(1):111-119, 1980.

Biological effects of chlorpromazine in chronic schizophrenics were investigated. Ss were 11 schizophrenics and 13 normal Ss. The doses of 0.2mg/kg of chlorpromazine were injected intramascularly into 11 schizophrenics and 8 normal men, and their blood samples were checked; the doses of 1.2ml to 1.4ml of physiological saline were injected intramuscularly into the other 5 normal men. Blood prolactin secretion in both groups increased after clorpromazine injection; the prolactin secretion of the schizophrenic group reached a maximum with a shorter latency period than that of the normal group after injection, and the growth hormone secretion in both groups increased after chlorpromazine injection. More cases of hyposecretion or hypersecretion were found among schizophrenics. The cortisol secretion was suppressed after chlorpromazine injection in both groups; thyroid stimulating hormone secretion showed no change. 29 references. (Author abstract modified)

003416 Kawahara, Ryuzo; Hazama, Hidebumi; Fukuhara, Tomokazu; Takeshita, Hisayoshi; Kayano, Masao; Hikita, Toru. Dept. of Neuro-psychiatry, Tottori University School of Medicine, Yonago 683, Japan **Biological effects of chlorpromazine in chronic schizophrenics. II. With reference to sympathetic neuronal function.** Kyushu Neuro-Psychiatry. 26(1):120-126, 1980.

Biological effects of chlorpromazine in chronic schizophrenics were investigated. Ss were 11 schizophrenics and 8 normal males who were injected with chlorpromazine and 5 normal males injected with physiological saline. The systolic blood pressure of schizophrenics showed significant elevation and paradoxical response as compared with the normal chlorpromazine group. The heartrate and wave height of the plethysmograph of the finger in both groups increased after chlorpromazine injection with no significant difference; the spontaneous galvanic skin response of schizophrenics was not suppressed after chlorpromazine injections. The spontanous galvanic skin response and the cortical level before chlorpromazine injection in schizophrenics had positive correlations with the degree of severity of schizophrenic symptoms. 25 references. (Author abstract modified)

003417 Kuschinsky, K. Abteilung Biochem. Pharmakol., MPI-Exp. Med., Gottingen, West Germany **/On the physiology and pharmacology of endorphins./** Zur Physiologie und Pharmakologie von Endorphinen. Klinische Wochenschrift. 57:701-710, 1979.

The physiology and pharmacology of endorphins were studied in reference to their possible therapeutic values. Endorphins are peptides with an opiate effect which are synthesized in several tissues of the organism, especially in the digestive tract and the central nervous system. Endorphins show a pharmacological spectrum of effects similar to classical opiates, especially in the analgesic area. Among other places, endorphins are located at strategically important spots of the central nervous system, and under certain circumstances they regulate the perception of pain. Possible effects of endorphins on the genesis of schizophrenic psychoses still are being studied. (Journal abstract modified)

003418 Leckman, James F.; Maas, James W.; Heninger, George R. Yale University Child Study Center, 333 Cedar St., New Haven, CT 06510 **Covariance of plasma free 3-methoxy-4-hydroxyphenethyleneglycol and diastolic blood pressure.** European Journal of Pharmacology. 70(2):111-120, 1981.

Plasma levels of the norepinephrine metabolite 3-methoxy-4-hydroxyphenethyleneglycol (MHPG) and blood pressure variables were measured in six fasting normotensive male Ss after clonidine (1 and 5mcg/kg) or placebo in a double-blind study. Plasma MHPG reached a nadir significantly below baseline and placebo level 3 hours after the 5mcg/kg clonidine dose. Mean MHPG concentrations were significantly correlated with diastolic blood pressure, but this relationship was independent of clonidine dose and sampling time. A significant correlation between plasma free MHPG and diastolic blood pressure was also found under drug free conditions. 49 references. (Author abstract modified)

003419 Massarotti, Marino; Allegri, Graziella; Roccella, Paolo; De Antoni, Antonio; Costa, Carlo; Toffano, Gino. Neurosurgical Clinic University, Arcispedale S. Anna, Ferrara, Italy **Levels of 5-hydroxyindoleacetic acid and tryptophan in lumbar cerebrospinal fluid and blood of patients with dementia and normal pressure hydrocephalus after tryptophan administration.** In: Amaducci, L., Aging of the brain and dementia, vol. 13. New York, Raven, 1980. 326 p. (p. 227-234).

The lumbar cerebrospinal fluid (CSF) concentration of 5-hydroxyindoleacetic acid (5-HIAA) after tryptophan (TRY) loading in patients with normal pressure hydrocephalus (NPH) and in controls was evaluated to determine any difference in conditions in which 5-HIAA production is stimulated. TRY load causes an increase of 5-HIAA levels in CSF mediated by an increase of serotonin biosynthesis in the brain. The lumbar CSF TRY concentrations and total and free TRY levels in serum before and after TRY load were measured in order to correlate metabolite levels with serum and CSF TRY levels. Ss included 10 patients with idiopathic NPH (presenting dementia with idiopathic communicating hydrocephalus) and 14 controls; all Ss had normal CSF pressure and normal composition. An oral dose of L-TRY (50mg/kg) was administered to each S. No difference in levels of total and free TRY in serum and of TRY in CSF were found after the amino acid loading between the idiopathic NPH Ss and the controls. The TRY load in NPH patients produced an increase in 5-HIAA levels in lumbar CSF significantly inferior to those of controls. It is suggested that the slight increase of 5-HIAA in CSF of NPH patients after loading does not depend on the availability of blood free or total TRY nor on interference with its active transport across the blood-brain barrier; instead, the hypothesis of reduced hydroxylation of TRY in idiopathic NPH Ss is supported. The regulation of serotonin biosynthesis in the brain is considered and the results provide evidence of the lowered activity of TRY-hydroxylase in idiopathic NPH. 32 references.

003420 McKeith, Ian G.; Williams, Anne; Nicol, A. R. Winterton Hospital, Sedgefield, Cleveland, England **Clonidine in Tourette syndrome.** Lancet. No. 8214:270-271, 1981.

A double-blind placebo controlled trial using clonidine in a 13-year-old boy with Tourette syndrome is reported. Clonidine (3mg/kg) produced no side-effects and reduced the number of motor and vocal tics. Progressive increases in dose lessened the therapeutic effect. Return to the original dosage was accompanied again by improvement, which had been maintained in a 3 month followup.

003421 Olanow, C. Warren; Finn, Andrew L.; Prussak, Charles. P.O. Box 2905, Duke University Medical Center, Durham, NC 27710 **The effects of salicylate on the pharmacokinetics of phenytoin.** Neurology. 31(3):341-342, 1981.

The effects of salicylate on the pharmacokinetics of phenytoin were investigated in six epileptic patients receiving long-term phenytoin therapy. Acetylsalicylic acid reduced the total serum phenytoin concentration but did not alter the free serum concentration. There was no loss of seizure control or toxicity. Total phenytoin concentrations in such patients may not accurately reflect pharmacologic activity and may be misleading. Aspirin appears to displace phenytoin from protein binding sites, thereby increasing availability for metabolism. It is considered unlikely that common analgesic dosages of aspirin would adversely affect the average phenytoin treated patient. 10 references. (Author abstract modified)

003422 Parkes, J. D.; Schachter, M.; Marsden, C. D.; Smith, B.; Wilson, A. King's College Hospital, London SE5 9RS, England **Lisuride in parkinsonism.** Annals of Neurology. 9(1):48-52, 1981.

Motor and hormonal changes associated with the dopamine receptor agonist, lisuride, were investigatd in nine Ss with idiopathic, postencephalitic, or drug induced parkinsonism. Lisuride is a soluble ergolene derivative with endocrine effects similar to, but more potent than, those of bromocriptine. Lisuride at a dosage of .05 to .15mg intravenously caused an immediate improvement in tremor, rigidity, akinesia, and postural deformity, but also caused chorea and orofacial dyskinesia. Improvement lasted 2 to 3 hr. Lisuride had little or no effect in a single patient with progressive supranuclear palsy. Oral lisuride therapy, .8 to 4.8mg daily, had similar effects but occasionally caused reduced awareness and hallucinations. Hormonal reactions were similar to those found for bromocriptine. 25 references. (Author abstract modified).

003423 Prikryl, P.; Rysanek, K.; Tovarek, J. 3rd Internal Clinic, Medical Faculty, University J. E. Purkyne, Dimitrova 14, 602 00 Brno, Czechoslovakia **Psychosomatic stress and lipoperoxides of human platelet-rich plasma.** Activitas Nervosa Superior. 22(4):300-301, 1980.

The effects of acetylosalicylic acid, indomethacine, and vitamine E on lipoperoxides in platelet rich plasma were investigated in normal human volunteers and in patients suffering psychosomatic stress reaction subsequent to myocardial infarction of ischemic heart disease. Significant differences were found between the lipoperoxide values before and after application of acetylosalicylic acid and vitamin E. No significant differences were found between the healthy Ss and the patients with psychosomatic stress reaction. 6 references.

003424 Puech, Alain J.; Brochet, Denis; Lecrubier, Yves; Simon, Pierre. Dept. de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris Cedex 13, France **/Neuroleptics: activation or inhibition of the dopaminergic system?/** Neuroleptiques: activateurs ou inhibiteurs du systeme dopaminergique? Psychologie Medicale. 12(11):2427-2430, 1980.

The effects (activation or inhibition) of neuroleptics on the dopaminergic system are discussed. The therapeutic effect of neuroleptic drugs seems related to the blockade of dopaminergic receptors. However, there are two types of dopaminergic receptors (DA-1 and DA-2) which could have opposite functions. The blockage of DA-1 receptors by drugs such as chlorpromazine inhibits the dopaminergic system, while the blockage of DA-2 receptors by drugs such as pimozide or sulpiride activates this system. Thus, it appears that neuroleptic drugs could have opposite effects on the dopaminergic system. 8 references. (Journal abstract modified)

003425 Rolandi, E.; Magnani, G.; Milesi, G. M.; Barreca, T. Via Montani, 32/4, I-1648 Genova, Italy **Effect of a psychoactive drug, trazodone, on prolactin secretion in man.** Neuropsychobiology. 7(1):17-19, 1981.

Trazodone, an antidepressant drug, was administered in a single oral dose (50 mg) to 10 normal Ss aged 24 through 41 years to determine its effect on prolactin secretion. A significant decrease of serum prolactin (PRL) values occurred. The mean serum PRL levels were 8.9 plus or minus 2.2ng/ml in basal conditions and 4.5 plus or minus 1.7ng/ml 180 min after trazodone. Pretreatment with this psychoactive drug does not modify TRH induced PRL release. 9 references. (Author abstract modified)

003426 Sachar, Edward J. Dept. of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY

10032 **Neuroendocrine approaches to psychoneuropharmacologic research.** In: van Praag, H., Handbook of biological psychiatry: part III. New York, Marcel Dekker, 1980. 383 p. (p. 169-177).

The neuroendocrine approaches to neuropharmacological issues are illustrated by a review of some recent studies of the hormonal effects of amphetamines and neuroleptics. Amphetamine studies include: the controversy about the relative effects of dextro-amphetamines and levo-amphetamines on brain noradrenergic and dopaminergic systems; the relative effect of the isomers on dopaminergic activity; and the effect of chronic D-amphetamine therapy in hyperkinetic children. Neuroleptic studies include: the relative prolactin (PRL) responses of normal subjects and schizophrenics to dopamine (DA) blockers and agonists as a way of testing the hypothesis of excessive brain dopaminergic activity in schizophrenics; the question of PRL response to neuroleptics in patients with tardive dyskinesia in whom a neuroleptic induced hypersensitivity of DA receptors has been hypothesized; the correlation between PRL responses and antischizophrenic properties of neuroleptics; drugs which are ineffective in schizophrenia; the question of PRL-stimulating potency in relation to clinical potency; and the neuropharmacological similarities and differences between three brain dopamine systems. 35 references.

003427 Sechter, Daniel; Briley, Mike S.; Raisman, Rita; Langer, Salomon Z.; Zarifian, Edouard. Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France / **3H-Imipramine binding in human platelets: diminution of binding sites in depressed patients.**/ Liaison de l'imipramine tritiee sur les plaquettes humaines: diminution des sites de fixation chez les deprimes. Psychologie Medicale. 12(11):2453-2457, 1980.

High affinity specific 3H-imipramine binding sites found in human platelets were studied. These binding sites were compared in 38 control subjects and 27 depressed patients before antidepressant treatment. Results indicate that the number of platelet binding sites in the depressed patients was significantly lower than in the control group. The affinity constants in the two groups were similar. The use of more subjects, more definite parameters, and postmortem studies on cerebral levels is suggested for future studies. 8 references. (Journal abstract modified)

003428 Seppala, T.; Linnoila, M.; Sondergaard, I.; Elonen, E.; Mattila, M. J. Dept. of Pharmacology, University of Helsinki, Helsinki, Finland **Tyramine pressor test and cardiovascular effects of chlorimipramine and nortriptyline in healthy volunteers.** Biological Psychiatry. 16(1):71-77, 1981.

The cardiovascular effects of chlorimipramine (CI) and nortriptyline (NT) were investigated in 20 healthy volunteer Ss, using a double-blind crossover design. Resting supine diastolic and systolic blood pressure (DBP and SBP) and heartrate were measured and tyramine pressor tests were performed. Main findings include: 1) both CI and NT shifted the dose response relationship for tyramine induced increase in SBP to the right; 2) this effect ocrrelated significantly with plasma desmethyl-CI but not with CI or NT concentrations; 3) CI increased both DBP and SBP at rest; and 4) NT increased heartrate at rest. Results are discussed with reference to previous studies of cardiovascular effects of tricyclic antidepressants and the relation of such effects to gender, age, and diagnosis of patient and the pharmacological profile of the drug. 25 references.

003429 Simpson, John A. University of Glasgow, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland **Baclofen: broader aspects of activity.** Scottish Medical Journal. 25(Baclofen Symposium Issue):S1-S2, 1980.

In an introduction to a symposium on baclofen, held in Glasgow in November, 1979, a brief history of the pharmacological treatment of paresis is presented preliminary to a discussion of baclofen. Recent evidence shows that (minus) baclofen is active, but the (plus)enantiomer is not. Like gamma-aminobutyric acid it inhibits dopaminergic systems and substance P, a polypeptide important in primary afferent transmission. The most important site of action is currently believed to be on the nerve terminals used for presynaptic inhibition. Implications of this action for potentiation of analgesic substances and for behavioral effects are considered.

003430 Small, Joyce G.; Milstein, Victor; Kellams, Jeffrey J.; Small, Iver F. Indiana University School of Medicine, Larue D. Carter Memorial Hospital, 1315 W 10th St., Indianapolis, IN 46202 **Auditory brain stem evoked responses in hospitalized patients undergoing drug treatment or ECT.** Biological Psychiatry. 16(3):287-290, 1981.

Brainstem auditory evoked responses (BSERs) were investigated in 24 psychiatric inpatients undergoing treatment with psychoactive drugs or ECT. Patients included those with diagnoses of schizophrenic disorders, major depressive disorder, bipolar disorder, schizoaffective disorder, and atypical psychosis; all but one ECT patient were receiving treatment with neuroleptics, tricyclic antidepressants, and/or lithium during the study period. Prior to therapeutic interventions, 85% of the BSER studies were interpreted as entirely within normal limits; this percentage remained unchanged during and following ECT and with drug treatment. One patient in each group had significant BSER abnormalities prior to treatment, but these disappeared before the time of the second recording; in three other patients, minor deviations were present which did not change with drug treatment or ECT. The one exception was in a 47-year-old depressed woman, who showed normal pretreatment BSERs, but whose recordings 24 hours after fifth seizure in the ECT showed remarkable deviations. 5 references.

003431 Surwillo, Walter W. University of Louisville, Health Sciences Center, Louisville, KY 40292 **Cortical evoked potentials in Gilles de la Tourette's syndrome -- a single case study.** Psychiatry Research. 4(1):31-38, 1981.

Average cortical evoked potentials (AEPs) to auditory stimulation and ARP recovery functions were investigated in a 13-year-old boy suffering from Gilles de la Tourette's syndrome. Data obtained from the patient while on and off haloperidol were compared with data from a group of normal control subjects matched for age and sex. Latencies of the P2 and N2 components of the AEP were noticeably shorter in the Tourette's syndrome patient than in the control group. Recovery from stimulation, as estimated by the cortical evoked potential to the second of two closely spaced stimuli, was faster in the patient than the controls. After the patient's treatment with haloperidol, the latencies of the P2 and N2 components of the AEP and the speed of recovery from stimulation appeared to be no different in the patient than in the control subjects. Findings suggest that cortical excitability is higher in the Tourette's syndrome patient, whose AEPs also showed evidence of a maturational advance over the normal subjects. 15 references. (Author abstract)

003432 Tyce, Gertrude M.; Sharpless, Nansie S.; Kerr, Frederick W. L.; Muenter, Manfred D. Dept. of Physiology, Mayo Clinic, Rochester, MN 55901 **Dopamine conjugate in cerebrospinal fluid.** Journal of Neurochemistry. 34(1):210-212, 1980.

Conjugated dopamine (DA) was detected in the cerebrospinal fluid (CSF) of two patients with Parkinson's disease during treatment with L-DOPA and an inhibitor of aromatic L-amino acid decarboxylase (L-AAAD). A DA conjugate probably DA sulfate was also detected in the CSF of dogs after administration of L-DOPA alone or in combination with an L-AAAD inhibitor. Conjugated DA in the plasma of dogs was reduced to a greater extent than free DA when an L-AAAD inhibitor was given with L-DOPA. This suggests indirectly that in the absence of enzyme inhibition the formation of DA sulfate conjugates is a rapid, efficient mechanism for the maintenance of low concentrations of free DA in plasma during L-DOPA administration. 18 references.

003433 Vajda, F. J. E.; Donnan, G. A.; Phillips, J.; Bladin, P. F. Dept. of Neurology, Austin Hospital, Heidelberg, Victoria 3084, Australia **Human brain, plasma, and cerebrospinal fluid concentration of sodium valproate after 72 hours of therapy.** Neurology. 31(4):486-487, 1981.

Sodium valproate concentrations were assayed in brain, plasma, and cerebrospinal fluid (CSF) of nine neurosurgical patients suffering from a variety of brain tumors. Sodium valproate was given for 3 days before surgery. Brain levels were 6.8% to 27.9% of plasma concentrations, and CSF levels were 7.6% to 25.0% of plasma levels. There was a significant correlation between brain and CSF levels and plasma on Spearman ranking. These results confirm that valproate is not selectively concentrated in brain fractions, and the concentration in brain is related to the free anticonvulsant level in plasma. 10 references. (Author abstract modified)

003434 Vidales, Juan Emilio. Hospital Nacional **/Endorphins./** Las endorfinas. Neuropsiquiatria. 10(2):73-82, 1979.

The effects of psychopharmaceuticals on endorphins are examined. Opium was one of the first substances used by man to mitigate a psychomotor excitation crisis. Opium is now utilized in experiments which attempt to discover the genesis of illnesses which affect the mind. The different endorphins (beta, gamma, alpha, mu, and delta) and their characteristics are presented. The endorphins are responsible for opiate behavior, analgesia, and violence. The discovery of endogenous substances with similar effects to opium creates new possibilities for investigation of cerebral neurotransmission. 12 references. (Journal abstract modified)

003435 Virtanen, Raimo. Dept. of Pharmacology, Institute of Biomedicine, University of Turku, Kiinamyllynkatu 10, SF-20520 Turku 52, Finland **Excretion of nortriptyline into saliva.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 19(2):78-81, 1981.

The relationship between serum and saliva concentrations of nortriptyline was studied in seven healthy volunteers given a single oral dose (50mg). The stimulation of saliva flow with Parafilm caused a significant increase in the mean saliva pH from 6.93 to 7.34. Simultaneously, the mean saliva/serum concentration ratio decreased from 0.28 to 0.14. This decrease correlated significantly with increases in flow rate and pH. As a result of the great variability in the saliva/serum ratios at any given pH, serum cocentrations could not be reliably calculated from saliva concentrations. 16 references. (Author abstract modified)

003436 Weir, Roger L.; Fan, Kuang J. Dept. of Neurology, Howard University College of Medicine, 2041 Georgia Avenue, NW, Washington, DC 20060 **Spinocerebellar degeneration with parkinsonian features: a clinical and pathological report.** Annals of Neurology. 9(1):87-89, 1981.

A clinical and pathological report is presented of a case of spinocerebellar degeneration with parkinsonian features in a 20-year-old Black female. Parkinsonian tremor improved with L-dopa treatment. Postmortem examination revealed posterior column atrophy in the spinal cord and severe degeneration in the substantia nigra. Atrophic changes were noted in deep cerebellar nuclei and superior cerebellar peduncles. This study confirms the relationships between clinical parkinsonism, substantia nigra degeneration, and the therapeutic effect of L-dopa. 8 references. (Author abstract modified)

003437 Zahn, Theodore P.; Rapoport, Judith L.; Thompson, Christine L. Bldg. 31, Rm. 4C39, NIMH, 9000 Rockville Pike, Bethesda, MD **Autonomic effects of dextroamphetamine in normal men: implications for hyperactivity and schizophrenia.** Psychiatry Research. 4(1):39-47, 1981.

The effects on autonomic nervous system (ANS) activity of two doses (0.25mg/kg and 0.50 mg/kg) of dextroamphetamine were tested in normal men. Skin conductance and heartrate were recorded during rest, tone presentation, and a reaction time task. Compared to placebo, dextroamphetamine increased both skin conductance and heartrate indices of arousal, slowed habituation, and reduced ANS responsivity selectively to more important versus less important stimuli. The last result differs from previous findings on hyperactive and normal boys. The pattern of ANS effects closely resembles findings on drug free schizophrenics, which suggests that it may be a marker for biological changes occurring in amphetamine psychosis and spontaneous psychotic episodes. 32 references. (Author abstract)

14 MECHANISM OF ACTION: BEHAVIORAL

003438 Akimov, G. A.; Medvedev, V. I.; Bakharev, V. D.; Zagryadskiy, P. V.; Stepovik, N. V.; Kaurov, O. A. Kafedra nervnykh bolezney, Voyenno-meditsinskaya akademiya im. S. M. Kirova, Leningrad, USSR **/Experience in using the hormones of the hypophysis posterior lobe in memory disturbances of varying geneses./** Opyt primeneniya gormonov zadney doli gipofiza pri narusheniyakh pamyati razlichnogo geneza. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(12):1787-1790, 1980.

Experience with the use of the hormones of the hypophysis posterior lobe in different types of memory disturbances was studied. Vasopressin and pituitrine were used in 20 patients (8 men and 12 women, 30 to 60 years old) with memory disturbances due to: circulatory disturbances of the vertebrobasilar system, atherosclerosis, neurasthenia, brain concussion, and epilepsy. A control group of 15 patients with memory disturbances due to cerebral atherosclerosis, neurasthenia, and epilepsy was used. The therapeutic efficacy of the hormones was evaluated by psychophysiological methods. Changes in the patients' neurological condition and subjective state were taken into account. Results show the therapeutic efficacy of the hormones in the treatment of amnesic syndromes and sleep disorders. These results indicate that there are no dangerous side-effects but that the treatment should not be used in pregnancy. 6 references. (Journal abstract modified)

003439 Bonnet, M. H.; Webb, W. B.; Barnard, G. no address **Effect of flurazepam, pentobarbital, and caffeine on arousal threshold.** Sleep. 1:271-279, 1979.

After laboratory and procedure adaptation, six normal Ss were administered randomly 30mg flurazepam (twice), 100mg pentobarbital (twice), 400mg caffeine (once), and placebo (twice) on nonconsecutive nights. On each night, Ss were aroused from standard segments of stage 2 sleep five to eight times with an ascending series of 1,000 Hz tones produced by an audiometer. Arousal threshold and awake threshold after each arousal were measured. Both thresholds were increased by flurazepam and pentobarbital and decreased by caffeine. All of the drugs appeared to modify arousal threshold in a time course fashion such that extreme effects were found during the first half of the night. However, the modifications of waking threshold by caffeine and flurazepam continued throughout the sleep period. The method may be a means of measuring the behavioral time course of drug activity during the sleep period. (Journal abstract)

003440 Caille, Jean-Emile. Centre d'Etude et de Recherche de Psychologie Appliquee, F-83800 Toulon, France **/Correlated study of the effects of SE-5023 in an hypoxic atmosphere on quantified EEG, vigilance, memory, and mood./** Etude correlee des effets du SE 5023 en atmosphere hypoxique sur l'EEG quantifie, la vigilance, la memoire et la thymie. Psychologie Medicale. 12(7):1589-1599, 1980.

The effects of the drug SE-5023 on EEG, vigilance, memory, and mood were studied. A sample of 12 subjects (6 in an anxiety state) was administered three separate treatments: 30mg of SE-5023 (almitrine plus raubasine), 10mg of almitrine, and 20mg of raubasine. Subjects were tested in an hypoxic atmosphere (15000 feet altitude). During these treatments, the subjects were tested for the effects on EEG, vigilance, memory, and mood. Results show that SE-5023 has an antihypoxic effect. SE-5023 returned the EEGs to normal, reduced acute psychomotor disturbances, improved memory, and reestablished good mood (decreased depression and anxiety). No harmful side-effects were noted. 5 references. (Journal abstract modified)

003441 Fourcade, Jacques; Bugat, Raymond; Favaro, Marc; Martin, Jean-Paul; Robert, Olivier; Thivel-Chamcham, Helene. Centre de Recherches due Service de Sante des Armees, 108, boulevard Pinel, F-69272 Lyon Cedex 1, France **/Comparison of the effects of four benzodiazepines on frame of mind and behavior in healthy subjects./** Comparaison des effets de quatre benzodiazepines sur l'etat et le comportement de l'homme sain. Psychologie Medicale. 12(10):2265-2277, 1980.

The influence of four different benzodiazepines on frame of mind and behavior in healthy subjects was studied. Clobazam, dipotassium clorazepate, diazepam, and lorazepam were administered to 40 healthy male and female subjects who were divided into two groups according to their level of axiety. Experimental conditions consisted of a visual and psychometric task performed for 4 hours over a period of 3 days, simulating a computer terminal professional activity. Results indicate that the drugs influenced the subjects to a certain degree, particularly in judgment, memorization, fatigue, and linguistics. 11 references. (Journal abstract modified)

003442 Gillman, M. A.; Lichtigfeld, F. J. 1032 Medical City, 106 Eloff St., Johannesburg, South Africa **A comparison of the effects of morphine sulphate and nitrous oxide analgesia on chronic pain states in man.** Journal of the Neurological Sciences. 49(1):41-45, 1981.

The effects of nitrous oxide and morphine sulphate on chronic pain states in man are compared. The similarity of effect indicates that nitrous oxide acts on the morphine receptor. In all cases where analgesia was produced, naloxone reversal occurred. These results provide additional evidence for a dual system hypothesis of pain perception and that nitrous oxide analgesia is mediated by the endogenous opiate system. In light of these findings, the possibility of using nitrous oxide to replace morphine sulphate as a screening test for deep brain stimulation analgesia is discussed. 8 references. (Author abstract)

003443 Gruzelier, John H.; Hammond, Nick V. Dept. of Psychiatry, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, England **Lateralized deficits and drug influences on the dichotic listening of schizophrenic patients.** Biological Psychiatry. 15(5):759-779, 1980.

Recall of dichotically presented digit strings was compared between normal Ss and 18 chronic schizophrenic patients tested over 12 weeks on chlorpromazine, placebo, and chlorpromazine reinstatement. Patients were subgrouped according to arousal (as indexed by orienting responses in a tone habituation sequence) and paranoid diagnosis. Digits were of equal intensity or differed by 20 dB between the ears and were reported in any order or one ear before the other. Overall, patients performed as well as control Ss, and withdrawal or reinstatement of drug did not reduce accuracy. Patient/control differences occurred when the louder digits were to be reported second and left hemisphere inhibitory mechanisms were involved, especially when patients were on chlorpromazine. Some lateralized differences in serial position effects found only in patients were interpreted as reflecting left hemisphere processing impairments. The more aroused patients showed poorer accuracy than the less aroused group due to reduced recall in the left ear. Paranoid patients had superior recall and showed less shifting of attenion away from the right ear than nonparanoids. Results are discussed in the context of neurophysiological theories of brain disturbance in schizophrenia. 60 references. (Author abstract)

003444 Iorio, G.; Infante, S.; Gritti, P.; Zizolfi, S.; Celani, T. I Facolta di Medicina e Chirurgia, Universita di Napoli, Napoli, Italy **/Flunitrazepam in the treatment of insomnia: a study of 50 psychiatric patients./** Il flunitrazepam (Roipnol) nella terapia dell'insonnia: studio su di un campione di 50 pazienti psichiatrici. Rivista Sperimentale di Freniatria. 103(2):412-425, 1979.

Insomnia, usually treated with hypnosis or minor tranquilizers, was studied using flunitrazepam. The sample of 50 patients, 21 men and 29 women (average age of 40) were classified on the basis of the diagnostic criteria of the World Health Organization (ICD-8) test. The sample consisted of 28 psychotics, 21 neurotics, and 1 patient with personality disturbances. Flunitrazepam was administered in doses of 2mg per day for a duration of 7 days. The evaluation of the hypnotic effect of the drug was considered through four variables: the time taken to fall asleep, sleep duration, depth of sleep, and the psychophysiological conditions upon waking. The data were evaluated statistically. The results indicate that the specific effect was good in 60%, average in 30%, and poor in 10% of the cases. 13 references. (Journal abstract modified)

003445 Johanson, C. E.; Uhlenhuth, E. H. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, 950 E. 59th St., Chicago, IL 60637 **Drug preference and mood in humans: repeated assessment of d-amphetamine.** Pharmacology Biochemistry and Behavior. 14(2):159-163, 1981.

Ten normal human volunteers participated in three identical choice experiments comparing preference for 5mg d-amphetamine and placebo. Each experiment consisted of nine sessions. During the first four sessions of each experiment, Ss received alternatively drug or placebo. During the next five sessions, they were given a choice between amphetamine and placebo. Subjective effects were assessed using the Profile of Mood States (POMS) before the drug was taken and 1, 3, and 6 hours later. Ss chose amphetamine an average of 4.0, 3.2, and 2.1 times out of 5 during each of the three experiments, in that order. Compared to placebo, amphetamine produced changes in mood as measured by the POMS, including increased vigor, elation, arousal, and positive mood. Mood changes produced by amphetamine were similar across all three experiments despite the decrease in drug preference, suggesting the independence of these two measures. Results are discussed in terms of developing methods for predicting the abuse potential of psychotropic drugs. 24 references. (Author abstract)

003446 Johnson, L. C.; Church, M. W.; Seales, D. M.; Rossiter, V. S. no address **Auditory arousal thresholds of good sleepers and**

poor sleepers with and without flurazepam. Sleep. 1:259-270, 1979.

Auditory arousal thresholds of 12 good and 12 poor sleepers (sleep onset insomniacs) were obtained during stage 2, stage 4, and REM sleep at various times of the night. Despite claims of being light sleepers who are easily awakened by noise, poor sleeper auditory arousal thresholds were the same as those of good sleepers. Flurazepam (30mg) administration increased the thresholds of six poor sleepers, but the increase was significant only during the period of peak effect which occurred 1 to 2 hours after ingestion. Consistent with poor sleeper complaints of trouble falling asleep, the return to sleep (i.e., sleep latency) was significantly longer for poor sleepers than for good sleepers following stimulus arousals during the first stage 2 and stage 4 periods of the night. Sleep latencies for good and poor sleepers did not differ significantly following subsequent arousals. The sleep latency following the first stage 2 stimulus arousal was reduced significantly in poor sleepers during flurazepam induced sleep. (Journal abstract)

003447 Kent, Saul. no address **Can drugs halt memory loss?** Geriatrics. 36(2):34, 36, 39-42, 1981.

The promise of vasopressin therapy in halting memory loss resulting from the aging process is examined. Recent evidence suggests that such therapy may alleviate memory impairment problems among patients suffering accidental brain trauma and major mental disorders, as well as in geriatric patients. Vasopressin is a hormone synthesized in the anterior hypothalamus of the brain and released from the posterior region of the pituitary gland. Research also suggests the role of the cholinergic system in learning and memory and the key function of the neurotransmitter, acetylcholine. The results indicate that a choline supplemented diet may help preserve memory, and future research should concentrate on the interaction between vasopressin and cholinergic mechanisms and the benefits of memory boosting therapies on life span. 20 references.

003448 Levy, Deborah L.; Lipton, Richard B.; Holzman, Philip S. Illinois State Psychiatric Institute, Chicago, IL **Smooth pursuit eye movements: effects of alcohol and chloral hydrate.** Journal of Psychiatric Research. 16(1):1-11, 1981.

Smooth pursuit eye movements (SPEM) were recorded in human volunteers prior to and after the administration of alcohol and chloral hydrate and quantified using a frequency analysis score previously employed in studies of schizophrenia. Single doses of 2.0 and 3.0ml/kg of alcohol and 1500mg of chloral hydrate resulted in SPEM disruption. Lower doses of these drugs failed to produce a significant measurable effect. The failure of doses of chlorpromazine in a previous study to disrupt SPEM considered together with the obvious disruption of SPEM by two CNS depressant drugs adds evidence that impaired SPEM in schizophrenics is not an artifact of neuroleptic treatment. A number reading task, known to normalize smooth pursuit impairments in schizophrenics, also significantly improved drug induced disruption. These findings weaken the interpretation that number reading improves pursuit only in the presence of poor motivation or inattentiveness. The sites of action of alcohol and chloral hydrate are discussed. 29 references. (Author abstract)

003449 Mello, Nancy K.; Mendelson, Jack H.; Kuehnle, John C.; Sellers, Margaret S. Alcohol and Drug Abuse Research Center, McLean Hospital, 115 Mill St., Belmont, MA 02178 **Operant analysis of human heroin self-administration and the effects of naltrexone.** Journal of Pharmacology and Experimental Therapeutics. 216(1):45-54, 1981.

The effects of maintenance on a narcotic antagonist, naltrexone, or placebo on patterns of operant acquisition and use of heroin were studied under double-blind conditions. Twelve male heroin addict volunteers lived on a clinical research ward for 34 days. After a 9 day drug free period, naltrexone or placebo were given and heroin was available for 10 days. Ss could earn money or heroin by responding on a second order schedule of reinforcement for approximately 90 min. Results demonstrate the feasibility of using direct measures of drug self-administration behavior to evaluate new pharmacotherapies for heroin abuse and indicate the effectiveness of naltrexone in suppressing heroin self-administration. 45 references. (Author abstract modified)

003450 Nakazawa, Yoichi; Hasuzawa, Hiroaki; Kotorii, Tatayu; Ohkawa, Toshihiko; Sakurada, Hiroshi; Nonaka, Kensaku; Dainoson, Keijiro. Dept. of Neuropsychiatry, School of Medicine, Kurume University, Kurume, Japan **Study on the effects of L-5HTP on the stages of sleep in man as evaluated by using sleep deprivation.** Folia Psychiatrica et Neurologica Japonica. 34(2):83-87, 1980.

The effects of L-5-hydroxytryptophan (L-5HTP, 200mg) on the EEG sleep pattern were investigated in normal Ss. When L-5HTP, 200mg, was orally administered, only percent S1 significantly decreased in comparison with baseline. There was no change in any sleep stage on the first recovery night. On the second recovery night, percent S1 significantly decreased, while percent REM sleep (SR) increased significantly. Slow-wave sleep (SWS) did not show any change. The effects of L-5HTP 200mg were investigated on the first recovery night following one night of sleep deprivation. SWS significantly increased on the first recovery night when a placebo was given, while this rebound increase of SWS disappeared and percent S2 significantly increased on the first recovery night when L-5HTP was given. Percent SR significantly increased on the next night after the L-5HTP night. 13 references. (Author abstract)

003451 Paty, Jacques; Brun, Alain; Brenot, Philippe; Gross, Christian; Claverie, Bernard; Gioux, Maxime; Deliac, Philippe. Hopital Pellegrin-Tripode, 2, place Amelie Raba Leon, F-33076 Bordeaux Cedex, France **/Capacities of attention, stress resistance, and slow cerebral potentials: effects of carpipramine on contingent negative variation waves and P-300./** Capacites d'attention, resistance au stress et potentiels lents cerebraux: effects de la carpipramine sur les ondes V.C.N. et P-300. Psychologie Medicale. 12(11):2373-2387, 1980.

The effects of carpipramine on attention, stress resistance, and slow event potentials were studied. Twelve voluntary, normal subjects were administered 150mg/day of carpipramine in a double-blind manner and were monitored to determine behavior, electrophysiology (P-300 and contingent negative variation event related potentials), and psychometric parameters and position. Results indicate that with typical therapeutic doses of carpipramine there was no effect upon awareness or attention, but contingent negative variation event related potentials were increased and situational effects were reduced. The main effect of the drug was found to be destruction of conditioning. Carpipramine effects vary according to an individual's reaction to stress. 35 references. (Journal abstract modified)

003452 Primrose, D. A. The Royal Scottish National Hospital, Larbert, Stirlingshire, Scotland **Self injury in subnormal patients.** Scottish Medical Journal. 25(Baclofen Symposium Issue):S44-S49, 1980.

A 21 month trial of the use of baclofen (lioresal) in mentally defective patients who exhibit self-injurious or other undesirable behavior is reported. The first observed effect was in the mood of the patients, who mostly became calmer and happier. Subsequently many showed a diminution in their undesirable behavior but hyperkinesis was not helped. A few patients maintained the improvement after stopping the drug, but in most it had to be continued, sometimes with an increase in dosage. Side-effects are discussed. 4 references. (Author abstract)

003453 Sanchez-Turet, M. Depto. de Psicologia Fisiologica, Universidad de Barcelona, Barcelona, Spain **/Effects of psychopharmaceuticals on driving capacity./** Efectos de los psicofarmacos sobre la capacidad de conduccion de automoviles. Revista de Psicologia General y Aplicada. 35(3):457-465, 1980.

The effects of psychoactive drugs on the capacity to drive automobiles are discussed. Certain drugs and the majority of psychoactive drugs affect the arousal level to the extent that driving skills are impeded. Given the amount of driving which almost every adult does, a review of literature on the subject is called for. The drugs which have been studied in the past include: heroin, LSD, marihuana, amphetamines, antidepressants, lithium salts, barbiturates, hypnotics, neuroleptics, and minor tranquilizers. Analysis of the research affirms that the majority of psychoactive drugs have a negative influence on the capacity and skillfulness needed to drive, causing a subsequent accident risk. 31 references. (Journal abstract modified)

003454 Smith, Christine M.; Swash, Michael. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, London, England **Effects of cholinergic drugs on memory in Alzheimer's disease.** In: Amaducci, L., Aging of the brain and dementia, vol. 13. New York, Raven, 1980. 326 p. (p. 295-304).

The effects of cholinergic drugs on memory function in Alzheimer's disease were investigated, along with the biochemical features of the disease and the role of postsynaptic receptors, the selectivity of neurotransmitter defect, and the relationship of neurotransmitter defect to symptoms. Findings from use of physostigmine with four Alzheimer's patients indicated that the memory defect is usually associated with changes in motivation and mood that affect the patient's response. To properly test the hypothesis that cholinergic drugs improve memory, it is necessary to take into account variations in severity and involvement of modality specific memory. Findings to date suggest the usefulness of boosting acetylcholine activity via the use of anticholinesterase drugs. 38 references.

003455 Spinweber, Cheryl L. Naval Health Research, Bldg. 36-4, Naval Regional Medical Center, San Diego, CA 92134 **Daytime effects of L-tryptophan.** Psychopharmacology Bulletin. 17(1):81-82, 1981.

To evaluate daytime hypnotic effectiveness of L-tryptophan, the effects of L-tryptophan on sleep latency, nap sleep stages, plasma tryptophan levels, and waking EEGs were assessed in 20 volunteer Ss. Results indicate that L-tryptophan (at a 4g dose) is an effective hypnotic when administered at times other than normal bedtimes. In both morning and evening administration, L-tryptophan significantly reduced time to sleep onset without producing changes in sleep stages. In addition, subjective sleepiness was significantly increased by a 4g dose administered at noontime in combination with a standard laboratory meal or during the early evening hours when administered alone. 13 references. (Author abstract modified)

003456 Staak, M.; Raff, G.; Nusser, W. Institute of Forensic Medicine, Nagelestr. 5, D-7400 Tubingen, West Germany **Pharmacopsychological investigations concerning the combined effects of dipotassium clorazepate and ethanol.** International Journal of Clinical Pharmacology and Biopharmacy. 17(5):205-212, 1979.

Reaction times were studied in 14 male Ss given a 20mg oral dose of dipotassium chlorazepate (DPC), with or without ethanol (1g/kg). After evening administration of DPC, optic reaction times were slightly increased and endurance and concentration were decreased. All types of performance tested were significantly impaired after DPC and ethanol, and this impairment was greater than that seen after ethanol alone. Performance levels had returned to near normal when Ss were retested the next morning. 29 references. (Author abstract modified)

003457 Starobinets, M. Kh.; Volkova, L. D. no address **/The neurophysiological and clinical aspects of pain./** Bol': neyrofiziologicheskiy i klinicheskiy aspekty. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(4):607-618, 1980.

The neurophysiological and clinical aspects of pain are discussed under the following headings: the peripheral mechanisms, the central mechanisms, the psychophysiology, the pathophysiology of pain in certain neurological syndromes, the treatment of pain syndrome, and methods of treatment which do not involve the use of drugs (hypnosis, acupuncture, etc.). The effect of certain substances, including serotonin, on the sensitivity of tissue to various stimuli is discussed, as is the capability of opiate like peptides to act as analgesics, and to evoke aggressive behavior. Attempts to introduce some objectivity into the measurement of pain, which is sometimes hampered by the subjective nature of much evaluation of pain, are also discussed. 146 references. (Journal abstract modified)

003458 Tell, Guy; Bohlen, Peter; Schechter, Paul J.; Koch-Weser, Jan; Agid, Yves; Bonnet, A. M.; Coquillat, Gilles; Chazot, Guy; Fischer, Catherine. Schechter: Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg Cedex, France **Treatment of Huntington disease with gamma-acetylenic GABA, an irreversible inhibitor of GABA-transaminase: increased CSF GABA and homocarnosine without clinical amelioration.** Neurology. 31(2):207-211, 1981.

Gamma-acetylenic GABA (GAG), a potent irreversible inhibitor of GABA-transaminase, was given orally in various dosage schedules to 14 patients with Huntington disease, and the biochemical effects of the drug on cerebrospinal fluid (CSF) concentrations of GABA and the GABA containing dipeptide, homocarnosine, were measured in 10 of 14 patients. Treatment with GAG increased CSF concentrations of GABA and homocarnosine as compared to pretreatment values, suggesting that the drug increased brain GABA concentration. Despite this neurochemical effect, the clinical state was not improved. Except for single seizure episodes in five patients, GAG therapy was well tolerated. These results do not exclude the possibility that agents that augment CNS GABAergic function may prove useful in therapy of Huntington disease. 27 references. (Author abstract modified)

003459 Walker, Mary K. University of Illinois, Medical Center, 845 South Damen Avenue, Chicago, IL 60612 **Effects of dextroamphetamine sulfate on repeated acquisition behavior and mood in humans: a preliminary report.** Psychological Record. 31(1):29-41, 1981.

The effects of nontoxic doses of orally administered dextroamphetamine sulfate on the learning behavior maintained by the repeated acquisition task in 4 healthy adult males were assessed. Subjects received either anhydrous dextrose placebo or 5, 10, or 15mg dextroamphetamine sulfate. Two hours after drug administration, subjects completed two repeated acquisition sequences and two self-report scales. Learning of the behavioral chains of the repeated acquisition task, using light position as a discriminative stimulus, was characterized by a decrease in errors and an increase in response rate which was maximal at a dose of 10mg drug. Subjective measures of drug effect on four mood clusters of the Profile of Mood States and five subscales of the Addiction Research Center Inventory demonstrate primarily a dose related function. 19 references. (Author abstract modified)

003460 Williams, Harold L; Rundell, Orvis, H., Jr.; Smith, Landgrave T. Dept. of Psychiatry, Oklahoma Center for Alcohol and Drug Related Studies, University of Oklahoma, P.O. Box 26901, Oklahoma City, OK 73190 **Dose effects of secobarbital in a Sternberg memory scanning task.** Psychopharmacology. 72(2):161-165, 1981.

Mean reaction times of 45 Ss obtained in a Sternberg memory scanning task were examined for the effects of secobarbital at two doses that span the range commonly used in clinical practice (1.47mg/kg and 2.94mg/kg). Both doses slowed reaction times significantly, with a more pronounced effect at the higher dose. The discriminability of the probe stimulus interacted with the barbiturate, producing a hyperadditive effect on reaction time, but only at the high dose. The data are interpreted as additional support for a hypothesis localizing the effects of secobarbital to stimulus encoding stages in the reaction process. 12 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

003461 Ananth, J. McGill University, Montreal, Quebec, Canada **Clinical aspects of dyskinesia.** Indian Journal of Psychiatry. 22(3):239-246, 1980.

Clinical aspects of tardive dyskinesia (TD), including predisposing factors, prevalence, precipitating factors, and reversibility are described and discussed. It is suggested that TD is not as prevalent as reported studies have indicated since these studies merely reflect the cumulative number of TD cases among the residual population of mental hospitals. Clinical and legal implications of treating a patient with neuroleptics which can produce TD are considered since the symptoms, however rare, are severe, incapacitating, iatrogenic, and treatment resistant. It is argued that such neuroleptics should be administered and that acute schizophrenic patients should not have the possible side-effects of their medication explained. 65 references.

003462 Bakris, George L.; Smith, Donald W.; Tiwari, Subash. 1026 East Wayne St., South Bend, IN 46617 **Dermatologic manifestations of lithium: a review.** International Journal of Psychiatry in Medicine. 10(4):327-331, 1980-81.

The major dermatological and immunological complications associated with lithium carbonate ingestion are summarized. This drug has demonstrated proven efficacy in the treatment of bipolar affective disorder. Lithium carbonate has been reported to cause folliculitis, pruritic dermatitis, acneiform eruptions, and psoriasis. The increased neutrophilic migration in the dermis induced by lithium may cause an increased cell division exacerbating preexisting psoriasis or inducing it in normal populations. An increased incidence of antinuclear antibodies has been found in psychiatric patients as opposed to controls, the greatest incidence being in those taking lithium. It is concluded that other than exacerbation of psoriasis and severe progressive acneiform eruptions unresponsive to treatment, dermatological manifestations are benign and do not warrant discontinuance of lithium carbonate. 26 references. (Author abstract modified)

003463 Bakris, George L.; Taylor, Michael A.; Mulopulos, George P.; Wawczk, Sandra. 1026 E. Wayne St., South Bend, IN 46617 **Lithium prophylaxis and the kidney.** Journal of Affective Disorders. 3(1):37-42, 1981.

The records of 44 patients under age 55 with bipolar affective disorders, who were without known systemic illness and who were receiving lithium prophylactically for a minimum of 6 months, were reviewed to determine the incidence of kidney related symptoms. Polyuria was the earliest and most frequent side-effect. Patients receiving other psychotropic medication in addition to lithium showed a significant increase in the prevalence of polyuria, particularly after 3 months of exposure to medication. The onset of polyuria was correlated with duration of lithium treatment and age at initiation of therapy. The data suggest that polypharmacy, duration of exposure to lithium and age each predict the development of delayed polyuria, a symptom consistent with interstitial nephritis. 36 references. (Author abstract modified)

003464 Barros-Pinto, Maria Coeli de. Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil **/Tardive dyskinesia./** A discinesia tardia. Jornal Brasileiro de Psiquiatria. 29(5):299-305, 1980.

The problems of tardive dyskinesia are examined. Tardive dyskinesia is internationally recognized as a severe side-effect of neuroleptic treatment. Despite all the knowledge about neuronal function and regulatory mechanisms, the hypothesis about hypersensibility of the post synaptic dopaminergic receptor does not allow for satisfactory therapeutic strategies. Due to these problems, the importance of prophylactic measures is emphasized. Some suggestions to relieve tardive dyskinesia include: suspension of medication, antidopaminergic treatment, cholinomimetic treatment, and GABA antagonist treatment. 7 references. (Journal abstract modified)

003465 Berger, Philip A.; Davis, Kenneth L. Stanford Psychiatric Clinical Research Center, V. A. Medical Center, Palo Alto, CA 94304 **Pharmacological studies of tardive dyskinesia: implications for future research.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 333-351).

Pharmacological studies of the drug treatment side-effect tardive dyskinesia are reviewed, and the many reasons a carefully designed, multicenter prospective study is needed to address the question of tardive dyskinesia are detailed. Areas covered include: epidemiology of tardive dyskinesia; differential diagnosis; neuropharmacology of tardive dyskinesia; pharmacological studies in humans with tardive dyskinesia; unanswered questions concerning tardive dyskinesia. The discussion that followed the presentation of the paper at a symposium for strategies for future research in schizophrenia is given. 87 references.

003466 Bersani, Giuseppe; Eliseo, Claudio; Nocera, Fabio; Dotti, Andrea; Hadjichristos, Christos; Tomasetti, Flavio; Galeazzi, Giancarlo. Istituto di Clinica Psichiatrica, Universita di Roma, Roma, Italy **/Tardive dyskinesia: clinico-epidemiological revision and contribution./** Discinesia tardiva: revisione e contributo clinico-epidemiologico. Revista di Psichiatria. 14(6):482-495, 1979.

The clinical features of tardive dyskinesia, as an extrapyramidal hyperkinetic symptomatology, resulting from chronic neuroleptic treatment, were studied. A sample of 170 subjects (86 men and 84 women) from a psychiatric hospital who had been receiving neuroleptic treatment for an extended period was categorized. Results indicate that 30.3% of the subjects demonstrated tardive dyskinesia. The majority presented slight dyskinesia, were over 60 years old, and had neuroleptic treatment for over 20 years. Some clinical ideas on prevention are proposed. 23 references. (Journal abstract modified)

003467 Bittencourt, P. R. M.; Richens, A. Clinical Pharmacology Unit, Institute of Neurology, Queen Square, London, WC1N 3BG, England **Anticonvulsant-induced status epilepticus in Lennox-Gastaut syndrome.** Epilepsia. 22(1):129-134, 1981.

A case report of a 22-year-old woman with the Lennox-Gastaut syndrome who developed serial apneic/tonic with concomitant bursts of repetitive spikes at 16 to 20/sec, after receiving therapeutic doses of chlormethiazole, clonazepam, and diazepam for the treatment of serial tonic/clonic generalized seizures is presented. A direct relationship was found between dose of chlormethiazole and frequency of apneic/tonic seizures. Since these tonic seizures have been noted during natural sleep and after sleep induced by various sedative drugs in patients with slow spike wave in the EEG, it is likely that the reduction in level of consiciousness induced by sedative drugs is the causative factor. 19 references. (Author abstract modified)

003468 Bodensteiner, John B.; Morris, Harold H.; Golden, Gerald S. Dept. of Neurology, Oklahoma Children's Memorial Hospital, University of Oklahoma, Oklahoma City, OK 73126 **Asterixis associated with sodium valproate.** Neurology. 31(2):194-195, 1981.

Two case reports of patients with asterixis who were taking valproic acid and had serum levels within the therapeutic range are presented. Asterixis is characterized by intermittent brief relaxation of tonically contracting muscles involved in the maintenance of posture. Neither patient had clinical or laboratory evidence of hepatotoxicity. Only one other patient has been reported with valproate associated asterixis in the absence of toxic serum drug levels of hepatotoxicity. Asterixis seems to be due to a central effect of the drug unrelated to hepatotoxicity or sedation. 15 references. (Author abstract modified)

003469 Branchey, Marc H.; Branchey, Laure B.; Richardson, Mary A. Rockland Research Institute, Orangeburg, NY **Effects of gradual decrease and discontinuation of neuroleptics on clinical condition and tardive dyskinesia.** Psychopharmacology Bulletin. 17(1):118-120, 1981.

The effects of a procedure for determining the lowest effective dose of neuroleptic medication, which involves gradual decrease and/or discontinuation of neuroleptics, on clinical condition and taradive dyskinesia were investigated in a group of 32 hospitalized chronic schizophrenic patients. Prior to the study period, neuroleptics were replaced in all patients by equivalent doses of loxapine hydrochloride, administerd in liquid form. In the experimental group, medication was decreased in successive steps of 5 weeks duration to one half, one fourth, and finally, one eight of its initial value. This was followed by the administration of a placebo medication for 6 months. Results indicate that 76% (n=16) of the experimental group relapsed; all but one of these deteriorated 2 to 14 weeks after medication was discontinued. The data support the effectiveness of low maintenance neuroleptic doses. Differential relapse rates by age, sex, and drug history are noted. 4 references. (Author abstract modified)

003470 Brasil, Marco Antonio Alves. Servico de Psiquiatria, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil **/Advantages and disadvantages of prolonged use of neuroleptics./** Vantagens e desvantagens do uso prolongado de neurolepticos. Jornal Brasileiro de Psiquiatria. 29(2):91-98, 1980.

The validity of prolonged use of neuroleptics for schizophrenics is discussed. Results of tests show that unwanted side-effects due to the prolonged administration of neuroleptics are not adequately known and therefore cannot be properly controlled. Patients taking neuroleptics should be monitored carefully, keeping these two aspects in mind. Withdrawal of the drug for short periods and the careful assessment of irreversible unwanted side-effects such as tardive dyskinesia should be routine practices. 19 references. (Journal abstract modified)

003471 Cancro, Robert; Davis, John M.; Klawans, Harold; Tancredi, Laurence. New York University Medical Center, 566 First Avenue, New York, NY 10016 **Medical and legal implications of side effects from neuroleptic drugs. A round-table discussion.** Journal of Clinical Psychology. 42(2):78-82, 1981.

In a round table discussion, the side-effects that may occur during the treatment of schizophrenia with neuroleptic drugs are fully examined. Included are autonomic, extrapyramidal, other CNS, endocrine, and metabolic, allergic, and skin and eye side-effects. The differences between the various side-effect profiles of various antipsychotic drugs are noted. The restrictions imposed by laws designed to protect the patient's rights are evaluated with regard to the side-effects of neuroleptic drugs. The meaning of informed consent is delineated. (Author abstract modified)

003472 Casey, Daniel E.; Korsgaard, Soren; Gerlach, Jes; Jorgensen, Aage; Simmelsgaard, Hans. Dept. of Psychiatry, V.A. Medical Center, 3710 SW US Veterans Hospital Road, Portland, OR 97201 **Effect of des-tyrosine-gamma-endorphin in tardive dyskinesia.** Archives of General Psychiatry. 38(2):158-160, 1981.

The effect of the nonopiate like beta-lipoprotein 62-77 fragment, des-tyrosine-gamma-endorphin (DTgammaE) in tardive dyskinesia was investigated in 10 chronic psychotic inpatients with neuroleptic induced tardive dyskinesia and parkinsonism who received DTgammaE and placebo. Drug effects on movement disorders and eye blinking rates were assessed by blind evaluations of randomly sequenced videotapes made during standardized examinations before and 30, 60, and 120 minutes after each injection and 24 hours postinjection of days on consecutive treatment. Changes in schizophrenic symptoms were evaluated openly with the schizophrenic subscale of the Comprehensive Psychiatric Rating Scale. There were no significant effects of DTgammaE on any parameter and no side-effects. This suggests that DTgammaE within the tested dose range does not influence the pathophysiology of neurolelptic induced dyskinesias or chronic schizophrenia and does not have neuroleptic properties. However, DTgammaE is well tolerated and should be tested with higher doses during prolonged treatment. 39 references. (Author abstract modified)

003473 Colt, Edward W. D.; Kimbrell, Diane; Fieve, Ronald R. Fieve: New York Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Renal impairment, hypercalcemia, and lithium therapy.** American Journal of Psychiatry. 138(1):106-108, 1981.

In view of recent reports of renal impairment and hypercalcemia associated with lithium treatment, concentrations of serum creatinine and serum calcium were determined in 97 manic-depressive patients treated at a lithium therapy clinic. Of these, two men had elevated serum creatinine and normal serum calcium levels, five women and one man had elevated serum calcium and normal serum creatinine levels, and one woman had both elevated serum creatinine and calcium levels. There was a trend for patients with elevated serum levels to be somewhat older than their counterparts with normal levels. Findings indicate that long-term lithium therapy was associated with only mild renal impairment and hypercalcemia and are consonant with previous findings. However, the mean duration of lithium treatment in these patients was only 44 months, it is possible that the prevalence of these disorders may increase with increased duration of therapy. 10 references.

003474 Crews, Eugene L.; Daw, Jane. University of Alabama in Birmingham School of Medicine, University Station, Birmingham, AL 35294 **Neuroleptic-induced syndrome mimicking myasthenia gravis.** Psychosomatics. 22(1):67-68, 1981.

A case study is reported of a 51-year-old schizophrenic woman who demosntrated symptoms of myasthenia gravis. Her symptoms included difficulty in swallowing, muscular weakness, and depression. Her prompt response to antiparkinsonism medication reversing her previous deteriorating course, implicated her neuroleptic medication as the cause of the syndrome. 8 references.

003475 Danielczyk, W. Neurologische Abteilung, Pflegeheim, Wien-Lainz, Austria /**Acute pharmacotoxic psychoses in chronic cerebral conditions.**/ Akute pharmakotoxische Psychosen bei chronischen zerebralen Erkrankungen. Wiener Medizinische Wochenschrift. 129 Suppl. 55: 1-15, 1979.

The psychopathological symptoms of acute pharmacotoxic psychoses in chronic cerebral disturbances are discussed, and an overview of their pathogenesis is given. The frequency of the occurrence of these psychoses in brain atrophy and degenerative brain disorders is noted. Patients with Alzheimer's disease and senile dementia, Huntington's chorea, multiple sclerosis, cerebrovascular disorders, and Parkinson's disease were studied, and the influence of various medications on the genesis of exogenous psychoses is discussed. Particularities in the treatment of Parkinson's disease are discussed in reference to pharmacotoxic psychoses. (Journal abstract modified)

003476 Davidson, Arnold B. Dept. of Pharmacology, Research Division, Hoffmann-LaRoche, Inc., Nutley, NJ **Animal models of tardive dyskinesia.** Psychopharmacology Bulletin. 17(1):45-47, 1981.

The development and utility of animal models of tardive dyskinesia are reviewed. Three types of animal models are described: homologous, analogous, and empirical correlational models. It is noted that the relationship between chronic treatment with dopamine receptor blockers and tardive dyskinesia has been studied by many investigators and has led to the development of two major types of animal models which may have utility in studying tardive dyskinesias. The supersensitivity model is partly homologous and partly analogous; the chronic cebus monkey model appears to be homologous to tardive dyskinesia in all respects. However, this latter model cannot be utilized extensively because of the time and expense involved. 13 references. (Author abstract modified)

003477 Davis, Kenneth L; Faull, Kym F.; Hollister, Leo E.; Barchas, Jack D.; Berger, Philip A. Psychiatry Service, V.A. Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468 **Alterations in cerebrospinal fluid dopamine metabolites following physostigmine infusion.** Psychopharmacology. 72(2):155-160, 1981.

The effect of intravenous physostigmine administration on the cerebrospinal fluid (CSF) levels of homovanillic acid (HVA) and dihydroxyphenylacetic acid (DOPAC) in normal Ss was determined. After an adjustment for differing CSF concentrations of probenecid, physostigmine was found to elevate CSF HVA and DOPAC concentrations. Results are discussed in relation to the ability of physostigmine to decrease the symptoms of some patients with tardive dyskinesia. The possibility that physostigmine may act indirectly to inhibit nigrostriatal dopaminergic impulse flow is mentioned. 71 references. (Author abstract modified)

003478 de la Fuente-Ramirez, Ramon. Instituto de la Nutricion, Mexico, D.F., Mexico /**Lithium carbonate and the kidney.**/ El carbonato de litio y el rinon. Salud Mental. 3(3):26-28, 1980.

The controversy surrounding the effects of lithium carbonate on the kidney is discussed. Some articles have suggested that lithium carbonate may be the cause of renal structural damage in some patients. The kidneys are the basic route for the excretion of this drug, but only about 20% is excreted. The doctor must make sure that patients taking lithium are on a low sodium diet or are taking diuretics. One common effect of lithium treatment is a diabetes syndrome. Although renal damage has been seen, it is possible that depressed patients taking this medication have a predisposition for renal problems. Doctors prescribing lithium carbonate should inform the patients of the danger, use a low concentration, and examine patients prior to taking the medication for adequacy of renal functions. A urine analysis should be done every 6 months. 16 references.

003479 Devane, C. Lindsay; Wolin, Richard E.; Rovere, Raphael A.; Panahon, Norma C.; Sutfin, Tamara A.; Jusko, William J. Jusko: Clinical Pharmacokinetics Lab., Millard Fillmore Hospital, 3 Gates Circle, Buffalo, NY 14209 **Excessive plasma concentrations of tricyclic antidepressants resulting from usual doses: a report of six cases.** Journal of Clinical Psychiatry. 42(4):143-147, 1981.

Six patients are described who achieved very high plasma concentrations of imipramine and desipramine during chronic therapy with usual doses. Side-effects were minimal. Speculation as to apparent tolerance includes the presence of low metabolite concentrations. It is concluded that plasma concentrations monitoring may be indicated to identify the occasional patient who achieves potentially toxic plasma concentrations while taking recommended doses of tricyclics. 16 references. (Author abstract)

003480 Dietz, Albert J., Jr. Dept. of Internal Medicine, University of North Dakota School of Medicine, Fargo, ND 58102 **Amphetamine-like reactions to phenylpropanolamine.** Journal of the American Medical Association. 245(6):601-602, 1981.

Cases of seven patients who experienced acute CNS effects following ingestion of phenylpropanolamine hydrochloride are reported. The drug is an amphetamine like substance that is found in 64 different over the counter preparations for colds and appetite suppression. It is also found in numerous prescription drugs. The effects seen in these patients range from stimulation of the medullary respiratory center to tremor, restlessness, increased motor activity, agitation, and hallucinations. Physicians are cautioned to note the possible side-effects from ingesting preparations containing phenylpropanolamine. 7 references. (Author abstract modified)

003481 Donaldson, James O.; Hale, Mahlon S.; Klau, Marc. Dept. of Neurology, University of Connecticut Health Center, Farmington, CT 06032 **A case of reversible pure-word deafness during lithium toxicity.** American Journal of Psychiatry. 138(2):242-243, 1981.

Observations of a pure word deafness in a patient during recovery from lithium induced delirium are reported. Pure word deafness, or the failure to comprehend the meaning of words in spite of perceived sound, is usually caused by bilateral posterior temporal lesions or a single lesion deep in the posterior lobe of the dominant hemisphere. The deficit in this case is attributed to lithium toxicity, and the aphasia was reversible in 2 days. Implications for the clinical use of lithium are mentioned. 10 references.

003482 Dunleavy, Raymond A. 1612 Greystone Place, Charleston, WV 25314 **Neuropsychological correlates of asthma: effect of hypoxia or drugs?** Journal of Consulting and Clinical Psychology. 49(1):137, 1981.

The effects of drugs on the neuropsychological test performance of asthmatic children were examined. No relationship was found between drug usage and test performance. These results are contrary to the hypothesis postulated by Suess and Chai that neuropsychological deficits in asthmatic children may be a function of certain antiasthama medication. 4 references. (Author abstract modified)

003483 Ezrin-Waters, Cheryl; Seeman, Mary V.; Seeman, Philip. Seeman: Dept. of Psychiatry, Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, Canada M5T 1R8 **Tardive dyskinesia in schizophrenic outpatients: prevalence and significant variables.** Journal of Clinical Psychiatry. 42(1):16-22, 1981.

All the patients of an outpatient clinic for schizophrenia were evaluated for the presence and severity of neuroleptic induced tardive dyskinesia. Forty four percent of the patients showed some degree of tardive dyskinesia. The proportion of patients with tardive dyskinesia increased directly with age and with number of years of neuroleptic treatment. Recent dose reduction exacerbated the syndrome. There were no gender differences in the clinic as a whole. Severity of dyskinesia correlated with anticholinergic drug use, with the piperazine/butyrophenone goup of neuroleptics and with the use of depot administered drugs. The depot correlation was highly significant in the under 30 age group. 38 references. (Author abstract)

003484 Friis, Mogens Laue; Broeng-Nielsen, Bodil; Sindrup, Erik Hein; Lund, Mogens; Fogh-Andersen, Poul; Hauge, Mogens. Dept. of Neurology, Frederiksborg Amts Centralsygehus, DK-3400 Hillerod, Denmark **Facial clefts among epileptic patients.** Archives of Neurology. 38(4):227-229, 1981.

The prevalence of facial clefts was determined in an unselected group of 3203 epileptic probands, and their personal data were cross-matched with a complete file of Danish facial cleft patients born between 1934 and 1977. Anticonvulsants have been suspected of teratogenicity, with facial clefts being the malformation most frequently associated with maternal anticonvulsant therapy. Paternal epilepsy has also been suggested as a factor in the genesis of birth defects, including facial clefts. An association between epilepsy per se and facial clefts would be reflected in a higher facial cleft prevalence among epileptics, and it consequently, would result in an increase of such malformations in their children. Eleven (11) epileptic probands had a facial cleft, which is twice the expected number. The increased prevalence of cleft defects among epileptics could partly explain why more of their children have facial clefts. 19 references. (Author abstract modified)

003485 Gardos, George. West-Ros-Park Mental Health Center, I.R.R. Room 323, 591 Morton Street, Boston, MA 02124 **Dystonic reaction during maintenance antipsychotic therapy.** American Journal of Psychiatry. 138(1):114-115, 1981.

Dystonic reaction during maintenance antipsychotic therapy (molindone) is reported in a 25-year-old male chronic schizophrenia outpatient. The S had been treated with a variety of neuroleptics over the 10 year course of his illness. Tardive dyskinesia was noted 2 years previously while the S was receiving 400mg/day thioridazine. Because of the patient's concern about tardive dyskinesia and obesity the thioridazine dose was gradually tapered and eventually discontinued, resulting in psychotic decompensation. Following hospitalization and reinitiation of neuroleptic therapy, the patient rapidly recompensated and was released on 90mg/day molindone. Because of moderately severe choreoathetoid dyskinetic movements, his dose was reduced to 75 and then to 50mg/day. A week later the patient showed a severe neurological reaction, with rigidity of the trunk, difficulty in arm movement, and an upward rolling of the eyes. Symptoms and subjective distress were relieved by administration of 2mg oral benzotropine. Choreiform movements were still evident at 6 week followup, but there was not recurrence of dystonic reactions. 4 references.

003486 Gilhus, Nils Erik; Aarli, Johan A. Dept. of Neurology, 5016 Haukeland Sykehus, Bergen, Norway **Respiratory disease and nasal immunoglobulin concentrations in phenytoin-treated epileptic patients.** Acta Neurologica Scandinavica. 63(1):34-43, 1981.

Symptoms of respiratory tract disease were recorded for half a year in 32 epileptic patients receiving phenytoin, and in 25 control Ss. There were 16 patients with normal IgA concentration in serum and nasal secretion, and 16 with a reduced concentration of IgA either in serum or in nasal secretion, or in both. Both groups of patients had significantly more frequent respiratory symptoms than did the control Ss. There was no difference when the patient group with decreased IgA concentrations was compared to that with normal IgA levels. All four patients with IgA deficiency both in serum and nasal secretion had, however, more frequent symptoms than any of the controls. There was no difference regarding respiratory tract disease in patients taking phenytoin only, compared to those combining phenytoin and other anticonvulsants. IgC and IgM levels in nasal secretion showed no direct relationship to the frequency of respiratory symptoms. 32 references. (Author abstract modified)

003487 Goldberg, Solomon C.; Shenoy, Ram S.; Sadler, Anne; Hamer, Robert; Ross, Beverly. Dept. of Psychiatry, Medical College of Virginia, Richmond, VA **The effects of a drug holiday on relapse and tardive dyskinesia in chronic schizophrenics.** Psychopharmacology Bulletin. 17(1):116-117, 1981.

The effects of a 6 week drug holiday on relapse, symptom status, and tardive dyskinesia in a group of chronically medicated schizophrenic patients were investigated. For 2 years prior to the study the 30 patients had been treated with fluphenazine decanoate, reporting to the clinic every 3 weeks for an injection. Prior to the 2 years on fluphenazine decanoate, they had been treated with a variety of other neuroleptics for varying periods of time (average duration of illness was about 13 years). Results indicte that the 6 week drug holiday is safe in that no patient relapsed; nor was there significant clinical worsening under the holiday treatment. On the contrary, there was a general improvement in global severity of illness over time. The initial low level of tardive dyskinesia among this sample did not change. 2 references. (Author abstract modified)

003488 Gordon, Christopher. Acute Psychiatry Service, Fruit Street, Boston, MA 02144 **Differential diagnosis of cimetidine-induced delirium.** Psychosomatics. 22(3):251-252, 1981.

A case history of a 60-year-old female patient with a differential diagnosis of cimetidine induced delirium is presented. Cimetidine was used for esophagitis. Since cimetidine is used to prevent stress ulcer in critically ill patients, the delirious patient often has several conditions that could cause a confused mental state. Like most confusional states, the syndrome of cimetidine induced delirium is nonspecific, having been reported to cause confusion, agitation, combativeness, unmanageability, hallucinations, stupor, coma, and convulsions, as well as depression and brainstem dysfunction. With this patient, mode of onset, intact memory, nondepressed mood, and normal vital signs differentiated cimetidine induced delirium from similar states. This case illustrates the clinical presentation of this form of confusion and the importance of differentiating it from similar states using ordinary history, physical examination, and laboratory studies. 10 references.

003489 Graze, Kathleen K. 2750 Broadway, Boulder, CO 80302 **Hyperparathyroidism in association with lithium therapy.** Journal of Clinical Psychiatry. 42(1):38-39, 1981.

A patient who was normocalcemic prior to treatment with lithium for manic-depressive psychosis is described, and his progressive hypercalcemia ensuing over the subsequent 6 years of therapy is reported. Elevated parathyroid hormone levels were found and neck exploration revealed a parathyroid adenoma. Unlike the usual case of hyperparathyroidism, the hypercalcemia was associated with a very low urinary excretion of calcium. The literature is reviewed and possible pathogenetic mechanisms are discussed. Serum calcium should be determined before and periodically during lithium therapy. It is concluded that in susceptible individuals, hypercalcemia may occur due to the unmasking or development of parathyroid adenoma. 9 references. (Author abstract)

003490 Haner, H.; Brandenberger, H.; Pasi, A.; Moccetti, T.; Hartmann, H. Gerichtl. Medizinische Institut, Universitat Zurich, Zurich, Switzerland /**Exceptional cases of death caused by tricyclic antidepressant agents.**/ Aussergewohnliche Todesfalle durch tricyclische Antidepressiva. Zeitschrift fur Rechtsmedizin. 84:255-262, 1980.

The controversy concerning the question of the effectiveness of tricyclic antidepressants is discussed. In view of the highly toxic nature of these drugs the question arises whether or not to replace them with less dangerous substances. The dangers of tricyclic antridepressants were documented during the investigation of 11 tricyclic poisoning cases in and around Zurich. Switzerland alone reported 54 tricyclic related deaths between 1967 and 1976. (Journal abstract modified)

003491 Harms, D. Kinderklinik, Universitat Erlangen-Nurnberg, West Germany /**Psychopharmaceuticals in pediatric practice.**/ Psychopharmaka in der Praxis des Kinderarztes. Medizinische Welt. 30:801-806, 1979.

The administration, side-effects, and dangers of psychopharmaceutical drugs for children are discussed. Tables listing the various psychotropic drugs and the most commonly used neuroleptic agents are provided. It is emphasized that psychopharmacotherapy should not be undertaken unless a comprehensive organic brain diagnosis has been made. Parents are warned not to have unrealistic expectations concerning the results of psychopharmacological treatment. Hereditory factors, the environment, and sickness all have an interacting effect on the outcome of drug therapy. Undesirable side-effects are reviewed, such as interference with mental functions, neurological disturbances (especially hypotonia and hyperkinesis), and vegetative disturbances. It is crucial to inform parents about possible side-effects resulting from administration of psychopharmaceuticals. (Journal abstract modified)

003492 Henderson, Victor W.; Wooten, G. Frederick. Aphasia/Neurobehavioral Unit, V.A. Hospital, 150 South Huntington Avenue, Boston, MA 02130 **Neuroleptic malignant syndrome: a pathogenetic role for dopamine receptor blockade?** Neurology. 31(2):132-137, 1981.

The neuroleptic malignant syndrome (NMS) of extrapyramidal signs and hyperthermia, an uncommon complication of therapy with the major tranquilizers is discussed. Other manifestations of NMS are pallor, diaphoresis, blood pressure fluctuation, tachycardia, and tachypneic hypoventilation, which may necessitate respirator support. Death often occurs, but full recovery can result with prompt recognition and proper management. In a patient with Parkinson disease and a chronic psychiatric disorder treated with haloperidol, typical features of NMS appeared upon cessation of dopaminergic antiparkinsonian drugs. Manifestations of NMS are attributed to dopamine receptor blockade in the striatum, increasing thermogenesis, and in the hypothalamus, impairing heat dissipation. 82 references. (Author abstract modified)

003493 Hoffman, Brian F. Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario M5T 1R8, Canada **The diagnosis and treatment of neuroleptic-induced parkinsonism.** Hospital & Community Psychiatry. 32(2):110-114, 1981.

Problems concerning the diagnosis and treatment of neuroleptic induced parkinsonism are discussed. Basal ganglia side-effects caused by neuroleptic drugs are frequently ignored, misdiagnosed, or mistreated by the patient or physician. Such side-effects must be anticipated and appropriate management instituted so that patient compliance with the drug regimen is increased and the therapeutic relationship is maintained. Side-effects can be detected in frequent and complete examinations of the head and neck, limbs, and chest and back. The various medications for drug induced parkinsonism are reviewed, with an emphasis on the indications for selection and the effects of each drug. Common errors in the diagnosis and management of the side-effects of neuroleptic drugs are summarized. 28 references. (Author abstract)

003494 Hoffmann, William F.; Ladogana, Loredana. 777 West End Avenue, New York, NY 10025 **Delirium secondary to clonidine therapy.** New York State Journal of Medicine. 81(3):382-383, 1981.

A case of delirium secondary to clonidine treatment in a 34-year-old Black male is reported. The patient, who had no previous history of psychiatric illness, suffered from vivid frightening dreams, and toxic delirium manifested by vivid hallucinations, delusions, impaired orientation, attentional deficit, and anxiety. There was no evidence that these symptoms were associated with alcohol withdrawal. An increase in the patient's dosage of clonidine 4 days prior to symptom onset, coupled with previous reports of hallucinations and delusions in patients taking clonidine, suggested that clonidine was the offending agent. Reduction of clonidine dose was associated with a gradual improvement in the patient's mental status over the following 4 days. Clonidine was discontinued and propranolol was substituted for control of hypertension. 5 references.

003495 Horrobin, D. F. P.O. Box 10, Nun's Island, Montreal H3E 1J8, Canada **Diazepam as tumour promoter.** Lancet. No. 8214:277-278, 1981.

Studies are briefly reviewed concerning the relationship between diazepam and the existence of tumors. Animal research indicates the possibility that diazepam might promote tumor activity. 8 references.

003496 Jackson, Ian V.; Davis, Leonard G.; Cohen, Ronald K.; Nuttall, Elizabeth A. Melbourne Clinic, 130 Church Street, Richmond, Melbourne, Australia 3121 **Lecithin administration in tardive dyskinesia: clinical and biomedical correlates.** Biological Psychiatry. 16(1):85-90, 1981.

Clinical and biochemical correlates of repeated oral lecithin administration were investigated in one male and five female chronic schizophrenia inpatients with manifest tardive dyskinesia (TD), using a double-blind crossover design. All Ss had been and continued to be maintained on a fixed dose of neuroleptic with no other psychoactive or anticholinergic medication. An increase in serum choline and an amelioration of TD ratings were associated with both 7 and 14 days of lecithin ingestion. Assessment of phosphatidyl choline levels showed no fluctuation over the seven serum samples for any patients; in all patients, an increase in phosphatidyl ethanolamine was evident in two reagent strips corresponding with lecithin ingestion. Dyskinesia and serum choline reverted to their original levels on ceasing lecithin. 21 references.

003497 Jackson, M. R.; Harris, P. A. Roche Products Limited, Welwyn Garden City, Herts AL7 3AY England **Absence of effect of diazepam on tumours.** Lancet. No. 8211:104, 1981.

The effect of diazepam on tumor growth was studied with rats for a 2 year period. Rats of each sex were used in each of four treatment groups receiving placebo or diazepam (1, 15, and 100 to 225mg/kg) daily by dietary admix. Survival was not adversely affected by diazepam. There was no evidence that diazepam enhanced spontaneous tumor growth in these animals and no indication of decreased latency in tumor induction that would suggest tumor growth promotion. The results do not support the suggestion by Horrobin et al. (1978, 1979, 1980) that diazepam may either cause or promote tumor growth. 4 references.

003498 Jefferson, James W.; Greist, John H. University of Wisconsin Center for Health Sciences, 600 Highland Avenue, Madison, WI 53792 **Some hazards of lithium use.** American Journal of Psychiatry. 138(1):93-94, 1981.

Clinical vignettes are presented that are representative, rather than comprehensive, examples of misadventure which may occur during the course of lithium therapy. These cases illustrate: 1) the importance of correct time sampling for the control of both manic and depressive aspects of bipolar depression; 2) the complications that may be caused by severe polyuria; 3) lithium treatment decision-making in patients with cardiovascular disease; and 4) and the failure to attend to clinical symptoms of lithium neurotoxicity as a result of too heavy reliance on laboratory findings indicative of therapeutic serum levels. The increasingly widespread use of lithium and its therapeutic potential in the treatment of manic-depressive illness have many benefits but, these will not be realized if the drug is used in a way that is haphazard, inattentive, or too rigid. Effort should be made to ensure patients treatment that maximizes the likelihood of response, minimizes side-effects and toxicity, and protects against iatrogenic complications. 8 references. (Author abstract modified)

003499 Jeste, D. V.; Neckers, L. M.; Wagner, R. L.; Wise, C. D.; Staub, R. A.; Rogol, A.; Potkin, S. G.; Bridge, T. P.; Wyatt, R. J. WAW Building, Room 536, Saint Elizabeths Hospital, Washington, DC 20032 **Lymphocyte monoamine oxidase and plasma prolactin and growth hormone in tardive dyskinesia.** Journal of Clinical Psychiatry. 42(2):75-77, 1981.

Lymphocyte monoamine oxidase (MAO) activity and plasma prolactin and growth hormone concentrations were determined blind in 12 elderly, female psychiatric inpatients with tardive dyskinesia and 12 inpatients without tardive dyskinesia, matched for primary diagnosis (schizophrenia or organic brain syndromes) and with a similar duration of neuroleptic treatment. Chronic shcizophrenic patients with tardive dyskinesia had significantly lower lymphocyte MAO activity as compared with clinical controls. Organic brain syndrome patients with tardive dyskinesia did not differ from controls in the lymphocyte MAO activity. These results with MAO parallel earlier findings on platelet MAO. No significant differences were found between tardive dyskinesia groups and controls in the plasma prolactin and growth hormone concentrations. Possible implications of these findings are discussed. 14 references. (Author abstract modified)

003500 Jezierska, Aniela; Sinczuk-Walczak, Halina; Turska-Koeppe, Grazyna. Instytut Medycyny Pracy, ul. Teresy 8, Lodz, Poland **/The clinical dynamics of tetraethyl lead poisoning./** Dynamika obrazn klinicznego zatrucia czteroetylkiem olowiu. Psychiatria Polska. 14(2):133-136, 1980.

The clinical picture of tetraethyl lead poisoning was studied in six patients 20 to 46 years old. Their poisoning by tetraethyl lead was accidential, and they were treated in a psychiatric ward, in a toxicological ward, or both. The symptoms appear 12 hours to 12 days after the patients absorbed the toxic substance. Most of the patients were hospitalized only when they showed acute mental disorders. Only in one case did the development of mental disorder stop at the predelirious stage and only in one case did the psychotic picture show characteristics of schizophrenia. The other four patients died. 4 references.

003501 Kane, John; Struve, Frederick; Woerner, Margaret; Weinhold, Paul. Dept. of Psychiatry, Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Preliminary findings with regard to risk factors in the development of tardive dyskinesia.** Psychopharmacology Bulletin. 17(1):47-49, 1981.

Preliminary findings of a prospective study of risk factors associated with the development of tardive dyskinesia are reported. Of the 500 patients studied, 73% were under 30 years of age and 48% were exposed to neuroleptics for less than 1 year. To date, 20 cases of presumptive tardive dyskinesia have developed. To examine the relationship between cumulative neuroleptic exposure and the development of tardive dyskinesia, the 20 prospective cases were compared to 186 prospectively followed patients with no evidence of tardive dyskinesia. The only significant difference between the groups is mean drug exposure, with the tardive dyskinesia group exposed to neuroleptics for significantly longer than the comparison group. 5 references. (Author abstract modified)

003502 Koller, William C.; Weiner, William J.; Perlik, Stuart; Nausieda, Paul A.; Goetz, Christopher G.; Klawans, Harold L. Klawans: Dept. of Neurological Sciences, Rush-Presbyterian St. Lukes Medical Center, 1725 W. Harrison, Chicago, IL 60612 **Complications of chronic levodopa therapy: long-term efficacy of drug holiday.** Neurology. 31(4):473-476, 1981.

The long-term efficacy of drug holiday for ideopathic parkinsonism patients receiving chronic levodopa therapy was investigated. Chronic use of levodopa may be complicated by dyskinesias, on/off effect, or hallucinosis. Transient levodopa withdrawal (drug holiday) may increase motor responsiveness and decrease levodopa induced side-effects, and the improved state may persist for as long as 9 months. After 1 year, parkinsonian signs approached preholiday levels, and two of the patients required a second drug holiday; side-effects began to reappear 9 to 12 months after the holiday. Four of six patients with psychiatric complications remained free of hallucinations for the entire year. 22 references. (Author abstract modified)

003503 Kopera, H.; Fluch, N.; Harpf, H.; Klein, W. W.; Stulemeijer, S. M. Dept. of Experimental and Clinical Pharmacology, University of Graz, Universitatsplatz 4, A-8010 Graz, Austria **Cardiovascular effects of mianserin -- a comparative study with amitriptyline and a placebo in healthy subjects.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 18(3):104-109, 1980.

The cardiovascular effects of amitriptyline and mianserin were compared with those of placebo in a double-blind study of 18 healthy volunteers. Drug dosage was increased gradually to a maximum of 150mg for amitriptyline and 60mg for mianserin, and treatment lasted for 8 days. Neither antidepressant altered objective physical condition, intraocular pressure, blood variables, or urinalysis, and drug effects on blood pressure were neglible. The preejection period was prolonged in amitriptyline treated male SS, indicating a negative effect on myocardial contractility. Mianserin reduced the left ventricular and systolic volume, probably by increasing the ejection fraction. It is concluded that therapeutic doses of tricyclic antidepressants such as amitriptyline may produce untoward cardiac effects, whereas mianserin, a tetracyclic antidepressant, may even improve cardiac output. 18 references. (Author abstract modified)

003504 Lazarus, J. H.; John, R.; Bennie, E. H.; Chalmers, R. J.; Crockett, G. Dept. of Medicine, University Hospital of Wales, Cardiff, Wales **Lithium therapy and thyroid function: a long-term study.** Psychological Medicine. 11(1):85-92, 1981.

Clinical and biochemical analyses of thyroid function of patients who had been continuously receiving lithium carbonate for 6 months or more were conducted. Of the 73 patients, goiter was found in 37%, exophthalmos in 23%, positive thyroid autoantibodies in 24%, and abnormal thyrotropin releasing hormone in 49%. It is suggested that thyroid failure due to lithium is usually dependent on antibody mediated damage, and that it is unlikely that lithium has a direct effect on the hypothalamic pituitary axis. 44 references. (Author abstract modified)

003505 Le Bellec, M.; Bismuth, Ch.; Lagier, G.; Dally, S. Clinique Toxicologique, Hopital Fernand-Widal, 200, rue du Faubourg-Saint-Denis, F-75010 Paris, France **/Severe withdrawal syndrome after cessation of benzodiazepine treatment: six clinical cases./** Syndrome de sevrage severe apres arret des benzodiazepines: Therapie. 35(1):113-118, 1980.

Extremely severe withdrawal syndrome as observed in patients after ending treatment with benzodiazepines is discussed. The withdrawal symptoms, particularly convulsions and myoclonies are more prevalent in patients who were under treatment for several months or years. These symptoms appear 3 to 6 days after the treatment ends. One common characteristic is the slow development of the symptoms; insomnia occurs immedidately but the more serious manifestations may not appear for a week. In most cases, the patients were administered low regular doses of oxazepam and lorazepam. It is concluded that the withdrawal of benzodiazepines should take place much more slowly. 4 references. (Journal abstract modified)

003506 Lieberman, Jeffrey. Mount Sinai School of Medicine, One Gustave L. Levy Place, KCC1-South, New York, NY 10029 **Cholinergic rebound in neuroleptic withdrawal syndromes.** Psychosomatics. 22(3):253-254, 1981.

A case history of a 21-year-old man suffering withdrawal symptoms from neuroleptic medication is presented. A variety of symptoms including headache, diarrhea, perspiration, restlessness, nausea, and vomiting can occur following withdrawal. These syndromes are speculated to be partly related to the autonomic activity of the withdrawn antipsychotic drug and/or the concomitantly administered anticholinergic medication. They are exclusive of the range of symptoms cnsidered part of the tardive or persistent dyskinesia syndromes, and of the psychopathologic symptoms that may return upon neuroleptic withdrawal. This patient's symptoms had a gradual onset, rapidly worsened, and then persisted. The usual picture and the autonomic nature of the symptoms with the suspicion of gastrointestinal hyperactivity prompted the trial of benzotropine. It is likely that these withdrawal syndromes are best handled by gradual as opposed to abrupt withdrawal of neuroleptics, giving the body a chance to adjust various physiological mechanisms. 10 references.

003507 Lindenmayer, Jean-Pierre; Vargas, Pilar. 60 Remsen Street, Brooklyn, NY 11201 **Toxic psychosis following use of quinacrine.** Journal of Clinical Psychiatry. 42(4):162-164, 1981.

A case study is reported of a 16-year-old male who developed an acute toxic psychosis after quinacrine treatment. The patient required psychiatric hospitalization. Treatment consisted of supportive therapy with antipsychotic medication given only when extreme agitation was evident. He gradually returned to this former condition. The case is discussed in light of previously published clinical reports and experimental studies. It appears that quinacrine acts as a cortical stimulant, but the exact mechanism of its action on the central nervous system is not clear. 7 references. (Author abstract modified)

003508 Ling, Michael H. M.; Perry, Paul J.; Tsuang, Ming T. Tsuang: Dept. of Psychiatry, College of Medicine, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Side effects of corticosteroid therapy: psychiatric aspects.** Archives of General Psychiatry. 38(4):471-477, 1981.

Literature is reviewed in order to determine the characteristics of corticosteroid induced mental disturbances. It is concluded that while dosage may be correlated to the risk of developing mental disturbances, neither dosage nor duration of treatment seems to affect the time of onset, duration, severity, or type of mental disturbances. Euphoria, depression, and psychotic reactions are the common manifestations of corticosteroid induced mental disturbances. Females seem to be more prone to these disturbances than males. Patients with past mental illness are not necessarily predisposed to such disturbances. Corticosteroid induced mental disturbances are usually reversible on dose reduction or discontinuation of the drug. At present there are no simple models to explain the psychotic reactions, anxiety, or agitation seen in corticosteroid induced mental disturbances. 81 references. (Author abstract)

003509 Loney, Jan; Whaley-Klahn, Mary Anne; Ponto, Laura Boles; Adney, Kenneth. Dept. of Psychiatry, University of Iowa, Iowa City, IA **Predictors of adolescent height and weight in hyperkinetic boys treated with methylphenidate.** Psychopharmacology Bulletin. 17(1):132-134, 1981.

The effects of methylphenidate treatment of hyperkinetic boys on adolescent height and weight were investigated via examination of archival data concerning 85 Ss treated with methylphenidate. Two separte stepwise multiple regression analyses were performed to predict adolescent height and weight, respectively. Among Ss whose growth was measured an averge of 5 years after they began drug treatment, specific drug related predictors of both adolescent height and weight are: 1) severity of early weight and appetite suppression side-effects; 2) number and length of drug holidays; 3) duration of methylphenidate treatment; and 4) occurrence of nausea or vomiting as an initial side-effect. It is suggested that children who experience side-effects are the ones at-risk for growth suppression, rather than the children who are treated with high dosages of methylphenidate. 7 references. (Author abstract modified)

003510 Lotti, Marcello; Johnson, Martin K. Johnson: MRC Toxicology Unit, Woodmansterne Road, Carshalton, Surrey, England **Neurotoxic esterase in human nervous tissue.** Journal of Neurochemistry. 34(3):747-749, 1980.

The distribution of neurotoxic esterase (NTE) in the human nervous system was mapped, and the sensitivity of NTE and related esterases to organophosphorus esters was examined. NTE was highest in the cortex, particularly in the gray matter. NTE activity in spinal cord was one third that in cortex. Activity in the peripheral nervous system was low but significant. The sensitivity of human NTE to Paraoxon and Mipafox was similar to that reported for hen NTE, within a range of threefold. 15 references.

003511 Maltbie, Allan A.; Varia, Indira G.; Thomas, Nunilon U. V.A. Medical Center, 508 Fulton Street, Durham, NC 27705 **Ileus complicating haloperidol therapy.** Psychosomatics. 22(2):158-159, 1981.

A case study is reported of a woman suffering from paranoid schizophrenia who developed ileus from haloperidol therapy. The increases in total daily dosage of haloperidol resulted in increased anticholinergic complications. The discontinued use of haloperidol and additional treatment relieved the symptoms of ileus. It is concluded that the weight and age of a patient should be considered when determining the daily dosage of haloperidol, and a more conservative use of this high potency antipsychotic agent is recommended. 5 references.

003512 Mansheim, Paul. Woods Schools, Langhorne, PA 19047 **Phenytoin toxicity in a brain-damage adolescent: a case report.** Child Psychiatry Quarterly. 14(1):1-4, 1981.

The case of an 11-year-old male patient is presented whose history and clinical course illustrate that phenytoin toxicity in mentally retarded and brain-damaged individuals may present with striking emotional and behavioral symptoms while neurological symptoms may be very subtle. The child had suffered brain-damage as the result of an automobile accident. The prominence of decreased self-care skills as the course of phenytoin toxicity continued was striking. Nystagmus was noticed only when his general condition had improved and his phenytoin level was back in the therapeutic range. These points support the general impression in the literature that symptoms of phenytoin toxicity in the retarded and brain-damaged are likely to be quite different from what is described in other cases, and that loss of self-care skills and emotional symptoms, especially inappropriate euphoria, are often prominent in these populations. 4 references.

003513 Mignee, C.; Garnier, R.; Conso, F.; Efthymiou, M. L.; Fournier, E. Garnier: Centre Anti-Poisons de Paris, Hopital Fernand Widal, 200, rue du Fg St-Denis, F-75010 Paris, France **/Acute overdosage with flunitrazepam./** Intoxication aigue par le flunitrazepam. Therapie. 35(5):581-589, 1980.

Treatment of overdosage of flunitrazepam, a benzodiazepine, is discussed. Symptoms include ataxia and then drowsiness and coma. However, central nervous system depression occurs at much lower doses than with other benzodiazepines. Two peculiar symptoms noted in a few cases are bradycardia and oligopnea. Even in massive overdosage, recovery is usual under supportive therapy. Gastric lavage is the most effective treatment when done shortly after ingestion. Further treatment depends upon the particular signs shown. Hypotension should be treated with colloid. Deep coma and oligopnea necessitate assisted mechanical ventilation. Sinus bradycardia does not require specific treatment. Acceleration of flunitrazepam loss through the kidney by forced diuresis should be avoided because of the low proportion of active metabolites excreted in urine. It is concluded that there are few accidental acute intoxications in children and when they do occur they are much less severe than those in adults. 27 references. (Journal abstract modified)

003514 Mitchell, James E. Box 393 Mayo, University of Minnesota Hospitals, 420 Delaware Street S. E., Minneapolis, MN 55455 **Discontinuation of antipsychotic drug therapy.** Psychosomatics. 22(3):241-247, 1981.

An overview of the possible symptoms of withdrawal that can accompany the discontinuation of antipsychotic drug therapy is presented. Possible symptoms include: psychotic relapse, medical complaints, and dyskinetic movements. Psychotic relapse, if it occurs, may be delayed for months or years and can be detected by close patient followup. Medical symptoms, such as nausea, vomiting, and dizziness, are time limited. Tardive dyskinesia may appear during or after drug withdrawal, but this problem is not necessarily permanent. To minimize symptoms, antipsychotic drugs should be tapered gradually, and patients on an antiparkinsonism medication should continue it for at least a week after the antipsychotic drug is stopped. 30 references. (Author abstract modified)

003515 Muller-Oerlinghausen, B.; Drescher, K. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaum-Allee 36, D-1000 Berlin, 19, West Germany **Time course of clinical-chemical parameters under long-term lithium treatment.** International Journal of Clinical Pharmacology and Biopharmacy. 17(5):228-235, 1979.

No pathological changes in routine clinical and chemical parameters were found in 40 manic-depressive patients treated with lithium for 3 years. Approximately 1000 blood samples were evaluated for hemoglobin, leucocytes, electrolytes in serum, electrophoresis, alkaline phosphatase, and serum creatinine and urea. Patients treated with other psychotropic drugs in addition to lithium were also studied. 13 references. (Author abstract modified)

003516 Nausieda, Paul A.; Koller, William C.; Weiner, William J.; Klawans, Harold L. 1725 W. Harrison, Suite 915, Chicago, IL 60612 **Pemoline-induced chorea.** Neurology. 31(3):356-360, 1981.

A case report is presented in which acute chorea in a child followed ingestion of pemoline mesylate, a central stimulant used to treat children with minimal brain dysfunction. In guinea-pigs, in an experimental model of chorea, chronic administration of pemoline induced behavioral supersensitivity to other dopaminergic agonists. Pemoline is similar to both d-amphetamine and methylphenidate in altering central dopaminergic sensitivity, and may cause chorea by similar mechanisms. Chronic pemoline therapy may offer no significant advantage over therapy with other indirect dopamine agonists. 19 references. (Author abstract modified)

003517 no author. Adverse Drug Reactions Advisory Committee, PO Box 100, Woden, ACT 2606, Australia **Mianserin: a possible cause of neutropenia and agranulocytosis.** Medical Journal of Australia. 2(12):673-674, 1980.

Four episodes of neutropenia or agranulocytosis possibly caused by the tricyclic antidepressant drug, mianserin hydrochloride, were reported to the Australian Adverse Drug Reactions Advisory Committee during the first year of the drug's general availability in Australia. Brief reports of these four patients, two of whom were concurrently receiving phenothiazines, are provided. A small number of reports from other countries support the possibility of this association between hemotological disorders and mianserin. Further surveillance to assess this potentially serious side-effect is needed. 2 references. (Author abstract modified)

003518 no author. no address **Extrapyramidal disorders and borderline syndromes: eredoataxias and dementia.** Pharmacology. 22(1):61-92, 1981.

Abstracts of papers given at the sixth meeting of the Italian League against Parkinson's Disease and Extrapyramidal Disorders, held in Naples in October 1979, are presented. Extrapyramidal and borderline syndromes (eredoataxias and dementia) are discussed, including Friedreich's ataxia and Alzheimer's disease. Biochemical, morphological, electrophysiological, and clinical features of these disorders are described, and various pharmacological approaches to treatment are considered.

003519 no author. no address **Ca-diazepam link? No scientific takers so far.** Medical World News. 22(4):28, 30, 1981.

The controversy surrounding Dr. David F. Horrobin and his claim that diazepam (Valium) may promote cancer is discussed. Dr Horrobin studied the effect of diazepam and other thromboxane A2 inhibitors on the growth of transplanted mammary tumors in rats and found the tumor growth significant. Others argue that there is no data showing a correlation btween the use of Valium and the growth of tumors in humans.

003520 Papadakis, Nikolas; Mark, Vernon H. Harvard Neurosurgical Service, Boston City Hospital, Boston, MA **Intermittent decortication and progressive hyperthermia, hypertension and tachycardia following methylglucamine iothalamate ventriculogram.** Applied Neurophysiology. 43(1-2):59-66, 1980.

A case of intermittent decortication and progressive hyperthermia, hypertension, and tachycardia is reported in connection with the use of methylglucamine iothalamate as an agent for ventriculography in a stereotactic procedure. Although methylglucamine iothalamate issued infrequently since the initiation of computerized tomographic (CT) scanning, other water soluble contrast materials, such as metrizamide, are being used for both myelography and as an adjunct to demonstrate intracranial structures in conjunction with CT scanning. Metrizamide, like methylglucamine iothalamate, can produce seizures, if the concentration in the subarachnoid space is great enough. Although the reaction that occurred in this patient has not been reported with metrizomide, the possibility of a similar reaction exists. 1 reference.

003521 Pariser, Stephen F.; Reynolds, James C.; Falko, James M.; Jones, Bruce A.; Mencer, Deborah L. Jones: Dept. of Psychiatry, Ohio State University Hospitals, 473 West 12th Ave., Columbus, OH 43210 **Arrhythmia induced by a tricyclic antidepressant in a patient with undiagnosed mitral valve prolapse.** American Journal of Psychiatry. 138(4):522-523, 1981.

A case report is presented on mitral valve prolapse syndrome, a common cardiac disorder which occurred following treatment of a 26-year-old depressed woman with the tricyclic antidepressant, desipramine. The patient showed symptoms of ventricular arrhythmia while taking desipramine but had no signs of panic attack. It is suggested that such a syndrome should be considered when young and otherwise healthy patients develop cardiac arrhythmias while taking tricyclic antidepressants. Propranolol can control the symptoms but may lead to an increase in depressive complaints. 8 references.

003522 Peachey, John E.; Brien, John F.; Roach, Carol A.; Loomis, Christopher W. Addiction Research Foundation, 33 Russell St., Toronto, Ontario, Canada M5S 2S1 **A comparative review of the pharmacological and toxicological properties of disulfiram and calcium carbimide.** Journal of Clinical Psychopharmacology. 1(1):21-26, 1981.

The absorption, metabolism, and elimination of disulfiram and calcium carbimide and the mechanisms of reaction with alcohol are described, and implications of these data from clinical practice are discussed. The effects and limitations of the interaction between ethanol and disulfiram and calcium carbimide are discussed. Four areas of concern regarding toxicity are discussed, including medical complications of the reactions with alcohol, toxicity associated with repeated doses of disulfiram or calcium carbimide, possible interactions with other drugs, and acetaldehyde induced hepatotoxicity and cardiotoxicity. 106 references. (Author abstract modified)

003523 Porot, Maurice; Plenat, Michel; Citron, Dominique. C.H.U. de Clermont-Ferrand, Groupe Hospitalier Saint-Jacques, Place Henri-Dunant, F-63003 Clermont-Ferrand Cedex, France **/Hepatic side-effects of antidepressant medications./** Accidents hepatiques des medicaments antidepresseurs. Psychologie Medicale. 12(11):2351-2356, 1980.

Liver disturbances as side-effects of antidepressant medications are discussed. These types of disturbances are rare; they occur in about 1% of cases and are linked most often to monoamine oxidase inhibitors. These drugs are responsible for a cytolitic syndrome, and tricyclics frequently are found to be responsible for a cholestatic syndrome. The pathogenesis of such side-effects still is debated. The following factors are considered to have some involvement in these side-effects: the virus may be reactivated, allergy to the antidepressant drug may develop, and/or an enzymatic induction and a transformation of bodily or drug substances into active metabolites may result from antidepressant drug administration. (Journal abstract modified)

003524 Pringuey, Dominique; Yzombard, Genevieve; Charbit, Jean-Jacques; Portugal, Henri; Saingra, Serge; Frayssinet, Raymond; Milech, Titus; Dufour, Henri. Service de Psychiatrie, Hopital Sainte-Marguerite, F-13274, Marseille, France **Lithium kinetics during hemodialysis in a patient with lithium poisoning.** American Journal of Psychiatry. 138(2):249-251, 1981.

The lithium concentrations in plasma and erythrocytes of a patient with lithium intoxication were compared while the patient was receiving hemodialysis. The findings yielded data on the pharmacokinetics of lithium ion concentrations during hemodialysis in this type of patient. The elimination curve of lithium showed a fast decrease of plasma levels and erythrocyte concentration. No linear correlation was observed between the plasma levels and the erythrocyteplasma ratio, nor between erythrocyte levels and the ratio, partly because this ratio did not differ greatly with time. The findings also provide an experimental model that confirms the lithium extrusion process from red blood cells. 8 references.

003525 Rappolt, Richard T., Sr.; Gay, George R.; Farris, R. David. Gay: Hilo Medical Group, 1292 Waianuenue Ave., Hilo, HI 96720 **Phencyclidine (PCP) intoxication: diagnosis in stages and algorithms of treatment.** Clinical Toxicology. 16(4):509-529, 1980.

Three stages of phencyclidine intoxication are described in detail. Specific diagnostic and therapeutic procedures are outlined. Two case studies are included. 39 references.

003526 Ratey, John J.; Ciraulo, Domenic A.; Shader, Richard I. Shader: New England Medical Center Hospital, Dept. of Psychiatry, Box 1007, 171 Harrison Avenue, Boston, MA 02111 **Lithium and marijuana.** Journal of Clinical Psychopharmacology. 1(1):32-33, 1981.

A possible interaction between marihuana and lithium that resulted in elevated serum lithium levels is reported. It is hypothesized that the patient's marihuana intake (3 to 4 cigarettes per day) increased the lithium absorption secondary to decreased gut motility. The possible anticholinergic effects of marihuana are described, and the need for physicians to be aware of drug/drug interactions among adolescent patients is emphasized. 18 references.

003527 Reinisch, June Machover. Dept. of Psychology, Rutgers University, Busch Campus, New Brunswick, NJ 08903 **Prenatal exposure to synthetic progestins increases potential for aggression in humans.** Science. 211(4487):1171-1173, 1981.

In an examination of hormone mediated aggression in humans, 17 female and eight male Ss whose mothers were treated with synthetic progestins during pregnancy and their nonexposed sex matched siblings were administered a measure designed to estimate potential for verbal and physical aggressive behavior. Ss ranged in age from 6 to 18 years old. Ss exposed during gestation showed a significantly higher potential for physically, but not verbally, aggressive behavior than did their nonexposed siblings. Neither age nor birthorder showed any relation to physical aggression scores, but the expected male/female difference between unexposed Ss was found. There were no differences in IQ between exposed and unexposed siblings. Results provide support for the hypothesis that behavior is masculinized by exposure to synthetic progestins during the early stages of development. 42 references. (Author abstract modified)

003528 Rinne, Urpo K. Dept. of Neurology, University of Turku, Turku, Finland **Recent advances in the treatment of Parkinson's disease.** Acta Neurologica Scandinavica. 62(Suppl. 78):103-121, 1980.

A review of research in the pharmacological (levodopa and/or bromocriptine) treatment of Parkinson's disease is presented. Problems associated with chronic levodopa treatment are outlined, including daily fluctuations in performance, end of dose deterioration, dyskinetic disabilities, parkinsonian neurasthenia, and neuropsychological responses (increased frequency of confusion and hallucination and cognitive and emotional dysfunctions). Research in the area of morality (reduced) and responses of brain dopamine receptors to levodopa is summarized. The therapeutic efficacy and side-effects of bromocriptine are compared with those of levodopa, and therapeutic effects and side-effects of combined levodopa bromocriptine treatment are discussed. Preliminary research into the effects of opiate antagonists, synthetic enkephalin analogues, and vasopressin in the treatment of Parkinson's disease is noted. 85 references.

003529 Risch, S. Craig; Groom, Geoffrey P.; Janowsky, David S. Janowsky: Dept. of Psychiatry (M-003), University of California, San Diego, La Jolla, CA 92093 **Interfaces of psychopharmacology and cardiology – part two.** Journal of Clinical Psychiatry. 42(2):47-59, 1981.

In the second of a series on the interfaces of psychopharmacology and cardiology, the psychopharmacology of the major tranquilizers and the minor tranquilizers, sedatives, and hypnotics is reviewed with respect to their cardiotoxicity, cardiovascular side-effects, and drug/drug interactions. The major tranquilizers examined include the phenothiazines, thioxanthenes, butyrophenones, and reserpine. Among the minor tranquilizers, sedatives, and hypnotics, focus is on barbiturates and related drugs and the benzodiazepins. Management of cardiovascular complications of psychotropic overdose is discussed, as well as potential therapeutic uses of psychopharmacological medications in patients with cardiovascular pathology. 401 references. (Author abstract modified)

003530 Risch, S. Craig; Groom, Geoffrey P.; Janowsky, David S. Janowsky: Dept. of Psychiatry, University of California, San Diego, La Jolla, CA 92093 **Interfaces of psychopharmacology and cardiology – part one.** Journal of Clinical Psychiatry. 42(1):23-34, 1981.

The pharmacology of the major classes of psychoactive agents is reviewed. These include antidepressants (tricyclic antidepressants and monoamine oxidase inhibitors), lithium carbonate, major tranquilizers (phenothiazines, thioxanthines, butryophenones, reserpine), and minor tranquilizers, sedatives, and hypnotics (benzodiazepines and barbiturates). Their cardiotoxicity, cardiovascular side-effects, and drug/drug interactions are summarized. Management of the cardiovascular complications of psychotropic overdose is discussed as well as potential therapeutic uses of psychopharmacological medications in patients with cardiovascular pathology. 191 references. (Author abstract modified)

003531 Rovinskaya, S. A.; Revva, L. I. Otdeleniye psikhofarmakologii Khar'kovskogo NII nevrologii i psikhiatrii, Kharkov, USSR **/On sensory disturbances occurring during neuroleptic therapy./** O sensornykh narusheniyakh, voznikayushchikh pri neyrolepticheskoy terapii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(6):905-909, 1980.

Sensory disorders were studied in 48 female schizophrenic patients undergoing neuroleptic therapy. Both elementary (pain, temperature, tactile, vibrational) and complex (differential two point stimulation, selectivity of perception) forms of contact sensitivity were observed in the patients before, during, and after treatment. It was found that following a 5 to 14 day period of neuroleptic therapy, 34 of the patients showed some form of sensory disorder. The six patients who had exhibited such disorders even before therapy now showed aggravated or modified symptoms. The observed disorders were dynamic and bilateral and involved different brain levels. In patients who were later able to leave the hospital, motor extrapyramidal changes were more frequent than sensory changes. It is concluded that neuroleptic drugs had a direct influence on the sensory sphere, and that the sensory disorders which appeared during the treatment could be designated as a neuroleptical sensory syndrome. 26 references. (Journal abstract modified)

003532 Royzin, L. no address **/Various factors in the pathogenesis of pathological reactions observed in connection with the administration of psychotropic drugs./** Mnogofaktornost' patogeneza patologicheskikh reaktsiy, nablyudayemykh pri vvedenii psikhotropnykh sredstv. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(7):1097-1100, 1980.

Various factors in the pathogenesis of pathological reactions to psychotropic drugs were studied with reference to the case histories of 1,730 patients, anatomical autopsy studies of the CNS of humans, the results of experiments on 4,050 rodents and monkeys, and the results of experiments in vitro on the culture of nerve tissue and certain subcell fragments. The action of tranquilizers, certain stimulants and antidepressants (including lithium), narcotics and hallucinogens was examined neurohistologically, histochemically and with the aid of electron microscopy. Toxic reactions in people who had taken phenothiazine substances were determined in the form of neurological, mental and behavioral disorders, and changes in the internal organs. Also determined were the effects of toxic doses of chlorpromazine on the internal organs of animals. 39 references. (Journal abstract modified)

003533 Sampath, G.; Kumar, Y. Vikram; Narayanan, H. S.; Rao, B. S. Sridhara Rama. National Institute of Mental Health and Neuro Sciences, Bangalore, India **Lithium neurotoxicity at report.** Indian Journal of Psychiatry. 22(3):304-306, 1980.

A case of a young manic patient who developed severe neurotoxicity when on lithium alone is presented. Investigations did not reveal the presence of any infection, electrolyte imbalance, or rise in lithium level. The possibility of lithium producing neurotoxicity at therapeutic levels for as yet unknown reasons is pointed out. It is suggested that this element of risk be considered when starting lithium for therapy or prophylaxis of affective disorders. 7 references. (Author abstract)

003534 Schou, Mogens; Vestergaard, Per. Psychistric Hospital, Risskov, Denmark **Lithium and the kidney scare.** Psychosomatics. 22(2):92, 94, 1981.

The relationship between therapy and morphologic signs of kidney damage is discussed. Research on glomerular function, tubular function, and renal morphology is considered, and it is concluded that none of the results warrant radical changes in the use of lithium where it is indicated. Lithium treatment should continue to be used and should be based on three conditions: 1) careful instructions to patients about treatment principles and risks; 2) cooperation between physician and patient; and 3) systematic monitoring of the treatment with serum lithium determinations.

003535 Seeman, Mary V. Dept. of Psychiatry, University of Toronto, Toronto, Ontario, Canada **Tardive dyskinesia: two-year recovery.** Comprehensive Psychiatry. 22(2):189-192, 1981.

The natural progression of tardive dyskinesia (TD) under conditions of clinically appropriate neuroleptic maintenance was examined over a 2 year period in a sample of schizophrenic outpatients. Ss were individually managed: when possible they were placed on extended drug holidays ranging in duration from 4 weeks to 1 year; when drug free periods were not possible, neuroleptic doses were reduced, and depot fluphenazine was changed to either oral neuroleptics or depot fluphenazine. Of the 41 TD patients initially assessed, 36 were available for followup assessment. In 56% of these patients, TD was either not present or was markedly reduced since the initial assessment; in 14% the TD score was higher at reassessment. There were no differences between males and females in TD recovery, nor were there significant differences between patients on neuroleptic maintenance less than or more than 10 years or between patients on intermittent or steady neuroleptic maintenance. TD recovery was significantly more frequent in patients under 40 years old as compared with those over 40. 14 references.

003536 Shukla, G. D.; Sharma, U. C.; Mehrotra, A. N. M.L.B. Medical College, Jhansi (U.P.), India **Intraocular pressure changes following modified E.C.T.** Indian Journal of Psychiatry. 22(3):274-276, 1980.

Intraocular pressure changes following modified electroconvulsive therapy (ECT) with and without succinylcholine were studied in 60 cases. The pressure was found to rise in both conditions, though the rise was more marked and longer lasting when succinylcholine was used. Without succinylcholine, tension returned to baseline within 3 minutes, while with succinylcholine the tension remained significantly raised even after that period. It is suggested that one should be cautious in giving ECT to patients with glaucoma particularly to patients under succinylcholine chloride. 13 references. (Author abstract modified)

003537 Smith, James M.; Burke, Mary P.; Moon, Cheung O. Harlem Valley Psychiatric Center, Wingdale, NY **Long-term changes in AIMS ratings and their relation to medication history.** Psychopharmacology Bulletin. 17(1):120-121, 1981.

Long-term changes in tardive dyskinesia and their relation to medication history were examined in a large sample using the Abnormal Involuntary Movement Scale (AIMS). One hundred thirty nine schizophrenic inpatients were examined twice with the AIMS, with a 3 year interval between examinations. The sample consisted of 71 males and 68 females with an average age of 57 years and an average length of current hospitalization of 25 years. Significant increases in total AIMS scores and subscales for lips, jaw, and tongue movements were observed in the second AIMS examination. Changes in AIMS total scores were examined for each of four medication course groups: steady neuroleptic use; increased neuroleptic use; decreased neuroleptic use; and off neuroleptics. Significant increases in AIMS scores were found for both the steady neuroleptic and off neuroleptics groups. 8 references. (Author abstract modified)

003538 Suess, William M.; Chai, Hyman. Psychophysiology Dept., National Jewish Hospital, 1999 Julian Street, Denver, CO 80204 **Neuropsychological correlates of asthma: brain damage or drug effects?** Journal of Consulting and Clinical Psychology. 49(1):135-136, 1981.

The conclusions by Dunleavy and Baade regarding hypoxic induced neuropsychological deficit in asthmatic children are questioned and regarded as premature. Dunleavy and Baade concluded that their results support the notion of hypoxic induced brain abnormalities in asthmatic children, because loss of consciousness and prolonged cyanosis, which may occur during a severe asthma attack. It is concluded that the possibility of similar deficits as a function of certain antiasthma medications must be considered. 23 references. (Author abstract modified)

003539 Summers, William, K.; Kaufman, Kenneth R.; Altman, Frank, Jr.; Fischer, John M. University of Southern California School of Medicine, Los Angeles, CA 90053 **THA -- a review of the literature and its use in treatment of five overdose patients.** Clinical Toxicology. 16(3):269-281, 1980.

The use of 1,2,3,4-tetrahydro-5-amino acridine (THA) to treat five cases of intentional drug overdose is described. THA was effective in four of the five cases and had minimal side-effects and a longer duration of action than physostigmine. Relevant literature is reviewed, with particular attention to tricyclic antidepressant overdose and acute anticholinergic syndrome. 55 references.

003540 Supprian, U. Psychiatrische Universitats-Klinik, Hamburg, West Germany **/Emergencies in manic-depressive psychoses./** Notfalle bei manisch-depressiven Psychosen. Neurologie und Psychiatrie fur die Praxis. 5:76-79, 1979.

In a brief overview, suggestions for verbal emergency treatment of manic or depressive patients are given. Febrile hyperkinesis is discussed, with emphasis on the need for electroconvulsive treatment. The dangers of depressive apathy, with the accompanying refusal to accept food, are enumerated. Potential side-effects resulting from psychopharmacological treatment of these psychoses are discussed. (Journal abstract modified)

003541 Tandberg, Dan. University of New Mexico School of Medicine, 620 Camino de Salud, NE Albuquerque, NM 87131 **How to treat and prevent drug toxicity.** Geriatrics. 36(2):64-65, 69-73, 1981.

Techniques of diagnosing, treating, and avoiding problems of overdosing among elderly patients are discussed. It is contended that drug toxicity emergencies in the aged are frequently a result of age related differences in drug absorption, distribution, and elimination. Intentional overdose is comparatively unusual and occurs mostly among aged patients who suffer from organic brain syndrome, severe affective or psychotic states, or chronic alcoholism. Additional social risk factors include loneliness, bereavement, poor economic situation, loss of meaningful employment, poor personal relations, and serious physical illness. After recovery, psychiatric evaluation and treatment is essential. To prevent occurrences of accidental and intentional overdose, a definite diagnosis is necessary before instituting therapy rather than nonspecific treatment of multiple symptoms. 23 references.

003542 Thysell, H.; Brante, G.; Sjostedt, L.; Lindergard, B.; Lindholm, T.; Franzen, G.; Rorsman, B. Dept. of Nephrology, University Hospital, S-221 85 Lund, Sweden **Glomerular filtra-**

tion rate and calcium metabolism in long-term lithium treatment. Neuropsychobiology. 7(2):105-111, 1981.

Glomerular filtration rate (GFR) and calcium metabolism were determined in 29 consecutive patients on long-term lithium therapy for 2.5 to 12 years and in four patients with lithium induced polyuria. In the consecutive series, the GFR was not significantly reduced and no correlations were found between this parameter and the duration of lithium therapy, average serum lithium, highest serum lithium noted, diuresis, or any of the calcium parameters. It is concluded that a relatively well managed lithium therapy for up to 12.5 years does not seem to influence the GFR, even if renal biopsy of four of the patients revealed interstitial nephritis and data in the literature indicate a progressive interstitial nephritis. Results do not support the proposition that polyuria is an alarming sign of pronounced renal lesion. Calcium metabolism is influenced by lithium therapy but from the clinical point of view no negative effects could be found. It is recommended that serum calcium be checked regularly in patients on long-term lithium therapy. 15 references. (Author abstract modified)

003543 Tyrer, Peter; Rutherford, David; Huggett, Tony. Mapperley Hospital, Porchester Road, Nottingham NG3 6AA, England **Benzodiazepine withdrawal symptoms and propranolol.** Lancet. No. 8219:520-522, 1981.

The effects of propanolol on benzodiazepine withdrawal symptoms were examined in 40 patients seen in general practice and psychiatric outpatient clinics who had taken lorazepam or diazepam alone in regular dosage for a mean period of 3.5 years. Ss had their benzodiazepine replaced by propanolol (60 to 120mg/day) or placebo for 2 weeks under double-blind conditions. Depending on the criteria for the definition of an abstinence syndrome, 27% to 45% of the patients had withdrawal symptoms during the study. Propranolol did not affect the dropout rate or the incidence of withdrawal symptoms, but did significantly reduce their severity in patients completing the study. The percentage fall in serum levels of desmethyldiazepam in patients who experienced withdrawal symptoms after stopping diazepam was significantly greater than in patients with no withdrawal symptoms. 19 references. (Author abstract modified)

003544 Uchigata, Masanobu; Tanabe, Hitoshi; Hasue, Ikuo; Kurihara, Masanao. Dept. of Neurology, Toranomon Hospital, Toranomon 2-2-2, Minato-ku, Tokyo 105, Japan **Peripheral neuropathy due to lithium intoxication.** Annals of Neurology. 9(4):414, 1981.

A case report of peripheral neuropathy due to lithium intoxication is presented. A 56-year-old man with a history of manicpsychosis who had been under intermittent treatment with lithium carbonate for 4 years developed drowsiness, dysarthria, tremor, and unsteady gait, followed by muscle twitching, increased muscle tone, sweating, and fever to 38 degrees C. Three months later dysarthria, truncal ataxia with mid limb ataxia, vertical nystagmus, mild weakness of the extremities, diminished deep tendon reflexes of the lower extremities, and decreased vibratory sense in the feet remained. The mild weakness, hyporeflexia, mild sensory deficits, and electrophysiological and histological findings in the case all are consistent with peripheral neuropathy. Temporal events incriminate lithium as the likely cause. 3 references.

003545 Uetrecht, Jack P.; Woosley, Raymond L. Woosley: Dept. of Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232 **Acetylator phenotype and lupus erythematosus.** Clinical Pharmacokinetics. 6(2):118-134, 1981.

Evidence for a relationship between acetylator phenotype and drug induced lupus erythematosus and idiopathic systemic lupus erythematosus is reviewed. There are several known therapeutic implications of acetylator phenotype; among them, the association of a higher incidence of procainamide induced and hydralazine induced lupus in slow acetylators. Presumably, this is because acetylation of the aromatic amine or hydrazine functional group leads to a nontoxic product. Several other drugs which have been implicated in drug induced lupus also contain an aromatic amine or hydrazine group. The clinical and laboratory characteristics of drug induced lupus and idiopathic lupus are similar, but the degree to which the pathophysiological mechanisms are related, if at all, is unknown. There is also evidence reported for an association between the slow acetylator phenotype and idiopathic lupus. If true, this relationship could provoke some new experimental approaches to investigation into the mechanism of idiopathic lupus. 136 references. (Author abstract modified)

003546 Versiani, Marcio. Av. N.S. Copacabana, 1133, conj. 1303, 22070 Rio de Janeiro, Brazil **/Therapeutics VI -- anxiolytics (benzodiazepines)./** Terapeutica VI -- ansioliticos benzodiazepinicos. Jornal Brasileiro de Psiquiatria. 29(5):307-312, 1980.

The therapeutic use of benzodiazepines is examined. All drugs in this class produce similar therapeutic and unwanted effects. Differences are seen basically in the half-life of the organism (oxazepam and lorazepam -- 8 hours; diazepam and chlordiazapoxide -- 24 hours). These drugs are most effective in neurotic, free floating anxiety which begins abruptly in a previously well adapted personality. The main side-effect is sedation; the drugs may be administered on a single, daily dosage schedule. Physical dependence is rare, but it may be suspected if unusual symptoms develop after suspension of the drug. 5 references. (Journal abstract modified)

003547 Vestergaard, Per; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Renal side effects of lithium: the importance of the serum lithium level.** Psychopharmacology. 72(2):203-204, 1981.

The importance of serum lithium levels as an indicator of renal side-effects of lithium was investigated in 19 lithium treated patients. It is noted that patients given long-term treatment with lithium often develop an impairment of renal water reabsorption which may lead to clinically significant adverse reactions. A convenient measure of this impairment may be obtained using the ratio of urine volume (V) divided by lithium clearance (CLi). When data from a large group of patients ($n = 218$) were recalculated, this ratio showed a significant correlation with the serum lithium level. This finding supports the suggestion that patients might be maintained advantageously at lower serum levels than those commonly employed. 5 references. (Author abstract modified)

003548 Weinhold, Paul; Wegner, James T.; Kane, John M. Kane: Dept. of Psychiatry, Long Island Jewish-Hillside Medical Center, P.O. Box 38, Glen Oaks, NY 11004 **Familial occurrence of tardive dyskinesia.** Journal of Clinical Psychiatry. 42(4):165-166, 1981.

Two case studies are reported of two brothers who had presumptive tardive dyskinesia. Both brothers exhibited abnormal involuntary movement with similar mental illness and treatment histories. This suggests the importance of examining neuroleptically treated relatives of an affected individual for dyskinesia, and indicates the possibility of a genetic factor in vulnerability. 8 references. (Author abstract modified)

003549 Whitelaw, A. G. L.; Cummings, A. J.; McFadyen, I. R. Division of Perinatal Medicine, Northwick Park Hospital and

Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England **Effect of maternal lorazepam on the neonate.** British Medical Journal. No. 6270:1106-1108, 1981.

The effect of maternal lorazepam on 53 neonates was examined for 5 days after delivery. In general, maternal plasma concentrations of lorazepam were higher than the corresponding cord plasma concentrations. Full-term neonates whose mothers had received oral lorazepam had no complications apart from a slight delay in establishing feeding, which in seven out of 29 cases was associated with relatively large doses of lorazepam. Intravenous administration of lorazepam for severe hypertension was associated with significantly low Apgar scores, need for ventilation, hypothermia, and poor suckling. Preterm babies whose mothers had been given lorazepam by either route had a high incidence of low Apgar scores, need for ventilation, hypothermia, and poor suckling. These babies had lower Apgar scores than those whose mothers had received diazepam, but the babies in the diazepam group were heavier and more mature. Lorazepam was an effective sedative and anxiolytic by either route, and there were no eclamptic fits among the lorazepam treated patients. The effects of lorazepam on neonates indicate that its intravenous use at any stage in pregnancy and oral use before 37 weeks should be restricted to hospitals with facilities for neonatal intensive care. 5 references. (Author abstract modified)

003550 Wieck, H. H. Universitats-Nervenklinik, Poliklinik, Erlangen, West Germany **/Changes in and current progress of neurology and psychiatry./** Wandel und aktuelle Fortschritte der Neurologie und Psychiatrie. Medizinische Welt. 30:334-341, 1979.

Changes occurring within the social structure and the nosological context with which psychiatrists are confronted are discussed. Progress in the areas of specific psychiatric diagnosis and therapy is described. Computer tomography is seen as a special diagnostic tool used to measure different degrees of functional psychoses with psychometric tests. The administration and side-effects of psychopharmaceutical drugs and other medications are analyzed for their potential neurological and psychiatric consequences. (Journal abstract modified)

003551 Witschy, James K.; Redmond, Franklin C. Redmond: Dept. of Psychiatry, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Dr., San Antonio, TX 78284 **Extrapyramidal reaction of fluphenazine potentiated by thyrotoxicosis.** American Journal of Psychiatry. 138(2):246-247, 1981.

Evidence of extrapyramidal reaction to fluphenazine potentiated by thyrotoxicosis in a 45-year-old patient mentally retarded schizophrenic is presented. The results are consistent with previous reports of such reactions in thyrotoxic patients treated with haloperidol, and the effects are probably due to interaction between the thyrotoxic state and neuroleptics in general. Implications for clinical use of antipsychotic medications to control behavior before a full organic evaluation can be completed are suggested. 4 references.

003552 Woogen, S.; Graham, J.; Angrist, B. Graham: Dept. of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **A tardive dyskinesia-like syndrome after amitriptyline treatment.** Journal of Clinical Psychopharmacology. 1(1):34-36, 1981.

A case report is presented of a 57-year-old woman who suffered orobuccolingual dyskinesia with associated dyskinetic movements of the hands which emerged rapidly during amitriptyline administration and which did not remit over 3 months of observations. This patient, who had only minimal prior exposure to neuroleptics, abruptly developed a syndrome clinically indistinguishable from tardive dyskinesia after only 4 days of treatment with amitryptyline at a dose of only 75mg/day. The dyskinetic movements did not remit over 3 months of observation after amitriptyline was discontinued. 11 references.

003553 Zarranz, J. J.; Caso, C.; Blanco, J. Seccion de Neurologia, Ciudad Sanitaria Sotomayor," Bilbao, Spain **/A trial treatment with tiapride for some extrapyramidal syndromes caused by neuroleptic agents./** Ensayo de tratamiento con tiapride de algunos sindromes extrapiramidales por neurolepticos. Actas Luso-Espanolas de Neurologia, Psiquiatria etc. 8(6):503-508, 1980.

Treatment with tiapride for patients with a combination of symptoms including Parkinson's disease, postural tremor, and orolingual dyskinesia caused by prolonged treatment with neuroleptics was studied. The 10 patients had chronic schizophrenia or paranoia, and a median hospitalization time of 21 years. All had received neuroleptic treatment for from 5 to 10 years, had a median age of 64, were in good health, and had a stable mental condition. Tiapride was administered in a dosage of 300mg per day. Results show a good tolerance for the medication, no side-effects, and some sleep improvement. There was no significant reduction in tremors, but there was no worsening of parkinsonism in most of the cases. 16 references. (Journal abstract modified)

16 METHODS DEVELOPMENT

003554 Aniline, Orm; Allen, Robert E.; Pitts, Ferris N., Jr.; Yago, Lane S.; Pitts, Andrew F. Dept. of Psychiatry, University of Southern California School of Medicine, Los Angeles, CA **The urban epidemic of phencyclidine use: laboratory evidence from a public psychiatric hospital inpatient service.** Biological Psychiatry. 15(5):813-817, 1980.

Results of a program for the routine assessment of phencyclidine (PCP) in blood of all newly admitted psychiatric patients in Los Angeles, California, are described. The procedure produced evidence that PCP exposure is frequent in these patients and may account for more psychiatric admissions than any other disorder. The gas chromatograph/nitrogen and gas chromatographic thermionic specific (nitrogen) detector methods are extremely sensitive for the detection of PCP, ketamine, and other arylcycloalkylamines, and trace amounts can be recognized. It is concluded that there is an urban epidemic of PCP abuse, use, and exposure. It is possible that 50 to 80 of the 135 patients studied would not have been admitted to the public psychiatric hospital if it were not for PCP. 13 references.

003555 Babbini, M.; Gaiardi, M.; Bartoletti, M. Institute of Pharmacology, University of Bologna, Italy **Effects of pentazocine and nalorphine on motility in chronically morphine treated rats: a potential substitution test to detect the narcotic character of a drug.** Neuropharmacology. 20(1):49-53, 1981.

Time effects of three doses of pentazocine and nalorphine upon locomotor activity were investigated in rats experimentally naive or treated chronically with 20mg/kg morphine daily. Pentazocine exhibited a motility pattern qualitatively similar to that of morphine. That is, in chronically treated rats acute depressive effects underwent tolerance, while acute excitatory effects became much more pronounced. Nalorphine, on the contrary, in no case exerted significant influence upon motility. These results, together with results obtained in previous work with methadone, meperidine, and methamphetamine, suggest that a locomotor activity substitution test might be a useful way to detect the narcotic character of a drug. 10 references. (Author abstract modified)

003556 Bondy, Brigitta; Remien, Jorg. Pharmakologisches Institut der Universitat Munchen, Nussbaumstrasse 26, D-8 Munchen 2, West Germany **Differential binding of chlorpromazine to human blood cells: application of the hygroscopic desorption method.** Life Sciences. 28(4):441-449, 19881.

Using a modified hygroscopic desorption method (HDM), the binding of chlorpromazine (CPZ) to human blood cells was investigated in the concentration range from 0.01 to 100mcmol/1. For erythrocytes and ghosts, the ratio between cell bound and free drug concentration was constant up to 60mcmol/1 CPZ. Saturable binding, however, was observed for lymphocytes, granulocytes and less pronounced for platelets. In contrast to red cells, CPZ binding to white cells and platelets was strongly dependent on pH. For all blood cells, a sharp decrease in binding occurred at drug concentrations higher than 60mcmol/1. This can hardly represent a true saturation of binding sites, since membrane damaging effects occur at these concentrations. Results suggest that binding of CPZ to erthrocytes represents an interaction at the water membrane interphase. For the different binding pattern of white cells, the cell organelles, the cytoplasma and the different composition of the membranes might be of importance. 17 references. (Author abstract)

003557 Branconnier, Roland J.; DeVitt, Donald; Cole, Jonathan O. Geriatric Psychopharmacology Laboratory, Boston State Hospital, Boston, MA **Evaluation of drug efficacy in dementia: a computerized cognitive assessment system.** Psychopharmacology Bulletin. 17(1):4-6, 1981.

A microcomputer based, cognitive assessment system for use in drug efficacy studies in senile dementia is described. At present, the following discrete cognitive processes test paradigms have been incorporated into the microcomputer system: Sperling's perceptual trace; Buschke's selective reminding task; depth of verbal encoding; digit/symbol recognition; Sterbnerg's item recognition; nonverbal incidental learning; and visual reaction time with variable foreperiod. The patient station consists of a Sanyo 15[illegible] computer remote terminal for presentation of visual display, a custom designed alpha numeric keyboard with special circuitry for accurate chronometric measurement of response time, and a Nutone intercom for verbal responses. 12 references. (Author abstract modified)

003558 Cossum, P. A.; Roberts, M. S. School of Pharmacy, University of Tasmania, Hobart, Tasmania, Australia **Availability of isosorbide dinitrate, diazepam and chlormethiazole, from i.v. delivery systems.** European Journal of Clinical Pharmacology. 19(3):181-185, 1981.

The loss of isosorbide dinitrate, diazepam, and chlormethiazole from aqueous solutions stored in plastic infusion bags and/or infused through plastic giving sets was investigated. During simulated infusions, the loss of isosorbide dinitrate was found to be flow rate dependent. The clinical and pharmacokinetic significance of this loss is discussed. Infusion of isosorbide dinitrate from a glass syringe through high density polyethylene tubing overcame the loss associated with its administration via plastic infusion bags and intravenous giving sets. This method was also applied successfully to minimize the previously reported loss of diazepam and chlormethiazole during infusions. 6 references. (Author abstract modified)

003559 Goldberger, Etienne; Cotonat, Jean; Boubli, Serge; Blanc, Michel; Girard, Martine; Escande, Michel; Gayral, Louis. Service de Psychiatrie, C.H.R. Purpan-Casselardit, F-31059 Toulouse Cedex, France **/First results of an original method for measuring blood levels of antidepressants (amitriptyline and nortriptyline)./** Premiers resultats d'une methode originale de dosage des taux seriques d'antidepresseurs (amitriptyline et nortriptyline). Psychologie Medicale. 12(11):2471-2476, 1980.

A new method for measuring plasma levels of amitriptyline and nortriptyline was studied. A daily dose of 100mg/square meters of body surface (average daily dose 160mg) was administered to 21 patients with deep depression. Plasma levels of amitriptyline and its catabolite nortriptyline were measured during the steady-state period (9 to 12 days into treatment). Results indicate that endogenous depression and cyclic depression demonstrate a correlation between improvement and the plasma level of amitriptyline and nortriptyline, and between the improvement and the proportion of amitriptyline/nortriptyline in plasma evaluated by demethylation. 22 references. (Journal abstract modified)

003560 Herberg, L. J.; Wishart, T. B. Institute of Neurology, National Hospital, Queen Square, London, WC1N 3BG, England **Self-stimulation and locomotor changes indicating neuroletpic (thioridazine).** Neuropharmacology. 20(1):55-60, 1981.

The use of a paradigm involving self-stimulation and locomotor changes to assess the anticholinergic potential of a representative noncataleptogenic neuroleptic, thioridazine, in comparison with that of a typical neuroleptic, spiroperidol, is described. Interactions of both compounds with a known anticholinergic agent, hyoscine, were also compared. Results are compatible with in vitro evidence that thioridazine exerts a powerful central anticholinergic action, masked in vivo by a simultaneous blockade of central dopamine receptors; this anticholinergic action would have preempted the action of hyoscine and accounted for the ineffectiveness of hyoscine after thioridazine; while partial reversal of the anticholinergic action, by oxotremorine, would have unmasked the dopamine blocking component of thioridazine and accounted for the accentuated depression of self-stimulation. These results support suggestions that blockade of acetylcholine receptors by thioridazine could contribute to its low liability to extrapyramidal side-effects in clinical use. 40 references. (Author abstract modified)

003561 Hogarty, Gerard E. Western Psychiatric Institute and Clinic, University of Pittsburgh, School of Medicine, Pittsburgh, PA **Natural and therapeutic environmental indicators of maintenance dosage requirements.** Psychopharmacology Bulletin. 17(1):36-37, 1981.

The utility of natural and therapeutic environmental indicators of maintenance dosages appropriate for pharmacological aftercare in schizophrenia is reviewed. The lack of precise data to guide maintenance therapeutic dosages is emphasized, and the need to consider the environmental demands upon the patient in adjusting dosage is examined. It is suggested that in benign environments medication requirements appear less than in stressful psychosocial environments. It is predicted that dosages might eventually be titrated, depending upon measures of personal and environmental vulnerability by concurrent application of human engineering principles. 12 references. (Author abstract modified)

003562 Koup, J. R.; Gibaldi, M. Dept. of Pharmacy Practice, University of Washington, Seattle, WA 98195 **Single point estimation of phenytoin dosing requirement.** Research Communications in Chemical Pathology and Pharmacology. 31(1):3-12, 1981.

Computer simulations showed that a single serum sample obtained 24 hours after a loading dose of phenytoin (18mg/kg i.v.) could predict the maintenance dose of phenytoin required to maintain a steady-state serum concentration of 15mg/L. A strong linear correlation was found between the required phenytoin maintenance dose and the reciprocal of the 24 hour serum concentration. The single point method of dosage estimation is not likely to be accurate, however, with oral dosage forms or when dosage requirements approach 10mg/kg/day. 12 references. (Author abstract modified)

003563 Le Normand, Y.; Kergueris, M.-F.; Lasserre, M.-P.; Plantard-Neau, C.; Larousse, C. Service de Pharmacologie, UER de Medecine, 1, rue Gaston-Veil, F-44035 Nantes Cedex, France **/Simultaneous administration of five antiepileptic drugs in plasma through gas-liquid chromatography./** Methode de dosage simultane de cinq anti-epileptiques dans le plasma par chromatographie en phase gazeuse. Therapie. 35(2):179-188, 1980.

The use of gas-liquid chromatography to determine plasma levels of antiepileptic drugs is discussed. After the removal of lipids by cyclohexane, the drugs are extracted by acidic dichloromethane, the solution is evaporated to dryness, and on column methylation occurs. The use of a heated nitrogen detector allows a single extraction procedure, avoiding the interference of plasma substances. Fast extraction and chromatography steps make possible more determinations per day. It is concluded that this technique will improve the use of these drugs; in epilepsy the dosage varies greatly and is difficult to determine. 16 references. (Journal abstract modified)

003564 Maziere, M.; Godot, J. M.; Berger, G.; Baron, J. C.; Comar, D.; Cepeda, C.; Menini, Ch.; Naquet, R. Service Hospitalier F. Joliot, Dept. de Biologie, CEA-Saclay, F-91190 Gif-sur-Yvette, France **Positron tomography. A new method for in vivo brain studies of benzodiazepine, in animal and in man.** Advances in Biochemical Psychopharmacology. 6:273-286, 1981.

A new method for in vivo brain studies of benzodiazepines in animals and humans, positron tomography, is described. The positrons and associated annihilation gamma rays emitted by carbon 11 make possible external visualization of intracerebral localization and quantitative measurement by positron emission tomography of the flunitrazepam labelled by carbon 11. With the use of carbon 11 as a tracer and the positron camera as an external detection device, it has been possible to study in a living baboon, with a noninvasive method, the cerebral and extracerebral kinetics of flunitrazepam and its in vivo interactions with other benzodiazepines. 17 references.

003565 Midha, K. K.; Cooper, J. K.; Lapierre, Y. D.; Hubbard, J. W. College of Pharmacy, University of Saskatchewan, Saskatoon, Saskatchewan, Canada **Fluphenazine, trifluoperazine and perphenazine in vacutainers.** Canadian Medical Association Journal. 124(3):263,265, 1981.

The possibility that contact of blood samples with the rubber stopper of the vacutainer tube may affect the measurement of the weakly basic lipophilic antipsychotic drugs, fluphenazine, trifluoperazine, and perphenazine was investigated using recently developed radioimmunoassay procedures for routine clinical monitoring. Duplicate blood samples, one of which was allowed to contact the stopper the other which was not, were collected from nine patients who received one of three drugs by intramuscular injection and from 27 patients who had received one of the three drugs orally. In seven of the nine samples of injected patients, drug concentrations in samples were significantly lower when the blood had touched the stopper. Substantial apparent reductions in plasma drug concentrations (.3% to 100%) were also found in patients receiving the medications orally. The need for clinicians to be aware of this problem is emphasized. 9 references.

003566 Mittel, Neuman S.; Gardner, George H., III; Rose, Betty W. Brockton V. A. Medical Center, Brockton, MA 02401 **Computerized monitoring of psychotropic drug orders: some trends and revelations.** Hospital and Community Psychiatry. 32(4):277-278, 1981.

The Drug Intake Management and Evaluations System, a computerized system to monitor psychotropic drug orders and provide feedback to physicians, was evaluated on three experimental hospital wards over a 10 month period. Drug orders were also monitored on two control wards where no feedback was provided. No significant differences were found between wards on any of the variables studied, due to a low incidence of improper drug usage. However, evidence was found that physicians who ordinarily are knowledgeable and careful in their psychopharmacologic practice may demonstrate significant deviation under duress. It was also found that the sophistication of the physician, not a monitoring system, was the most important single factor in determining the quality of psychopharmacologic practice. It is concluded that computerized monitoring may provide a safeguard against disturbances in ward milieu, as well as tangible proof of quality assurance efforts. 8 references.

003567 Molcan, J.; Rakus, A.; Zucha, I. Mickiewiczowa 13, 800 00 Bratislava, Czechoslovakia **/Some methodological ways of monitoring the effects of psychotherapeutic drugs./** K niektorym metodickym moznostiam sledovania ucinku psychofarmak. Ceskoslovenska Psychiatrie. 75(5):324-330, 1979.

A method of studying the effects of psychotherapeutic drugs was applied experimentally to 20 patients of a psychiatric clinic. In addition to their usual medication, the subjects received a pill containing the drug evaluate the effect of the drug by answering 20 items of a list of effects on a three point scale. Three parameters of the effects were defined: quality, consistency, and homogeneity. Each parameter is a measure of a different type of information about the drug's effect. It is concluded that the model experiment illustrates a method of determining the variety, homogeneity, and consistency of the effect of a drug. 3 references. (Author abstract modified)

003568 Muller-Oerlinghausen, B.; Renfordt, E. Dept. of Psychiatry, Eschenallee 3, Free University of Berlin, D-1000 Berlin 19, West Germany **Time-blind analysis and other video-strategies in phase II trials of psychotropic drugs.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 18(3):99-103, 1980.

The use of videotape techniques for psychiatric assessments in psychopharmacological trials is described. Videotapes of normal or specially structured interviews can be evaluated by more than one investigator and on a time blind basis, resulting in a more standardized average rater judgment. Analyses of videotapes of patients treated with mianserine, amitriptyline, or viloxamine are presented. 22 references. (Author abstract modified)

003569 Nyberg, G.; Axelsson, R.; Martensson, Erik. Martensson: Psychiatric Dept. III, Lillhagen's Hospital, S-42203 Hisings Backa 3, Sweden **Cerebrospinal fluid concentrations of thioridazine and its main metabolites in psychiatric patients.** European Journal of Clinical Pharmacology. 19(2):139-148, 1981.

A new gas chromatographic method for the determination of thioridazine and its metabolites in very low concentrations in cerebrospinal fluid (CSF) is described and illustrated by a study of CSF levels of thioridazine and its main metabolites in psychiatric patients. In the 48 psychiatric patients (who had received 40 to 1000mg/day of thioridazine), the total CSF concentrations of thioridazine and thioridazine side chain sulfone were significantly higher than their free serum concentrations whereas the total CSF concentration of thioridazine ring sulfoxide was significantly lower than its unbound serum concentration, and the total CSF concentration of the thioridazine side chain sulfoxide did not differ from its free serum concentration. The concentrations of thioridazine in serum and CSF varied significantly with age of patients, but no other correlation with age could be demonstrated in drug related parameters. The sex of the patients appeared to influence the side chain oxidation products, as the total CSF concentrations of the thioridazine side chain sulfoxide and side chain sulfone, as well as the free fraction in CSF of thioridazine side chain sulfoxide, were significantly higher in women. 5 references. (Author abstract modified)

003570 Ramsey, T. A.; Strand, S.; Stern, S.; Mendels, J. Dept. of Psychiatry, V.A. Hospital, Philadelphia, PA **MMPI prediction of imipramine response: a replication study.** Neuropsychobiology. 7(2):94-98, 1981.

The predictive validity for imipramine response of the MMPI was investigated. Eighteen hospitalized male depressives were treated with imipramine hydrochloride for 28 days. Prior to initiating treatment, each patient completed the MMPI. At the end of the treatment period, the patients were divided into groups of responders and nonresponders based on the change in Hamilton Depression Rating Scale scores. The Imipramine Response Scale - Male (IRS-M), a scale consisting of MMPI items, was scored for each patient and the ability of the scale to predict response or nonresponse in this sample was examined. Contrary to previous studies of the IRS-M, IRS-M scores did not predict imipramine response with better than chance accuracy. 7 references. (Author abstract modified)

003571 Viala, Alain; Durand, Alain; Grimaldi, Frederique; Cano, Jean-Paul. Laboratoire de Toxicologie generale et Biotoxicologie, 27, boulevard Jean-Moulin, F-13385 Marseille Cedex 05, France **/Therapeutic interest of blood levels determination for antidepressants: methodological approach./** Interest therapeutique de la determination des taux sanguins des antidepresseurs: approche methodologique. Psychologie Medicale. 12(11):2465-2470, 1980.

The possible prediction of the steady-state plasma levels of antidepressant drugs is examined. Through the influence of associated drugs or other compounds, a selective and sensitive method is developed for their determination. The method involves a selective extraction from whole blood or plasma, the use of an internal standard, and gas chromatographic analysis with a nitrogen selective detector. This method has general applications and may be used for pharmacokinetic investigations, for therapeutic control, and for analytical toxicology. 36 references. (Journal abstract modified)

003572 Wei, E. T. School of Public Health, Earl Warren Hall, University of California, Berkeley, CA 94720 **Enkephalin analogs and physical dependence.** Journal of Pharmacology and Experimental Therapeutics. 216(1):12-18, 1981.

A novel method of drug delivery, the osmotic minipump, was used to measure the ability of morphine and eight enkephalin analogs to produce physical dependence. After 3 days of morphine or peptide infusions into the rat brain, the dependent state was established and revealed by naloxone challenge; escape behavior, shaking, tachycardia, and an increased respiration rate provided objective evidence of withdrawal. The minipump method required only small amounts of test materials; 6mcg of morphine sulfate or 0.7mcg of FK 33,823, the most potent enkephalin analog, infused for 3 days per rat, were sufficient to induce dependence in all animals tested at these dose levels. A positive rank correlation was obtained between the short-term activities of the eight enkephalin analogs in inhibiting a motor response to a noxious stimulus and the long-term activities of the enkephalin analogs in producing physical dependence. 53 references. (Author abstract)

17 MISCELLANEOUS

003573 Achte, Kalle. no address **/Some observations on the psychological dimensions of placebo effects./** Einige Bemerkungen zu den psychologischen Dimensionen des Placebo-Effekts. Psychiatria Fennica 1979. 15-18, 1979.

The literature on placebo therapy and placebo effects in medicine and psychotherapy is reviewed. The primary and secondary effects of placebos used in psychopharmacological studies are discussed, with emphasis on the suggestive effects of placebos in behavioral change. The dynamics of placebo therapy are described, and the place of placebos in medical and psychiatric practice is defined. The occurrence of toxic reactions to placebo therapy also is examined. 18 references.

003574 Albou, Paul. Laboratoire de Psychologie economique, Universite Rene-Descartes, Paris V, France **/Self-medication./** L'automedication. Bulletin de Psychologie. 32(342):921-935, 1979.

Self-medication, its economic ramifications, and its psychosocial dimensions are discussed. Self-medication assumes a real or imagined pathological situation and entails the use of medicine without the intervention of a doctor. Although it is a universal phenomenon, self-medication is studied rarely. The economic ramifications of self-medication can be estimated by reviewing sales statistics of nonprescription drugs and of other home remedies. Self-medication can be motivated by the inaccessibility of the doctor, cost factors, or a dislike of the doctor-patient relationship, in which the patient assumes an inferior position. It is concluded that self-medication is in the public interest in cases of minor illnesses, because health services and doctors would tend to be available for more serious cases. It is suggested that general health education be improved so that the layman can distinguish more easily between major and minor illnesses. 28 references.

003575 Angelergues, Rene. Centre Philippe-Paumelle, 11, rue Albert-Bayet, F-75013 Paris, France **/The necessity of psychopharmacology in the development of psychiatry./** Necessite d'une psychopharmacologie pour l'evolution de la psychiatrie. Evolution Psychiatrique. 45(4):825-833, 1980.

The role of psychopharmacology in psychiatry's development is discussed. The use of chemotherapy in psychiatry has opened up new dimensions for the latter; however, clinical psychopharmacology has not been developed to the extent that experimental psychopharmacology has been developed on animals. It is thought that psychopharmacology as practiced daily in human chemotherapy should be subjected to a rigorous psychopathological analysis and that this will lead to a deemphasis of the present dichotomy between chemotherapies and psychotherapies. (Journal abstract modified)

003576 Barash, Harry Melvin. Saint Louis University **Drug and dietetic therapies for hyperkinetic children. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):3002-A, 1981. Ann Arbor, Univ. Microfilms No. 8100476, 101p., 1980.

Research trends from 1968 to 1979 concerning therapies for hyperkinetic children were reviewed. It is noted that trends from 1968 to 1973 revealed that studies began to yield more of needed controlled, quantitative data on which to base rational decisions regarding drug therapy for children with behavioral and learning disorders. The beneficial and harmful effects of medication were being documented. Trends from 1974 to 1979 documented the origination and follow through research of the thesis that hyperactivity is caused by artifical flavors and colors in food. Projective future trends emphasize the alternatives to drug and dietetic therapies. (Journal abstract modified)

003577 Battig, K. Institut fur Verhaltenswissenschaft, Eidg. Technische Hochschule, Turnerstrasse 1, CH-8092 Zurich, Switzerland **The smoking habit and psychopharmacological effects of nicotine.** Activitas Nervosa Superior. 22(4):274-288, 1980.

Psychopharmacological research into the effects of nicotine in typical smoker doses is reviewed in relation to the great difficulty in quitting smoking reported by habitual smokers. In addition to its positive psychopharmacological effects, nicotine appears to have no adverse psychological effects on the consumer, and the habit is supported by considerable sociocultural and biological dispositional factors. The absence of a general hypothesis of the manifold modes of action of nicotine is noted, and the role of dependence in the adverse effect experienced during short-term abstinence is discussed. The importance of nonnicotinic factors in maintaining smoking behavior is briefly noted. 76 references. (Author abstract modified)

003578 Bille, J. Service des Maladies du systeme Nerveux, Hopital Saint-Joseph, 26, boulevard de Louvain, F-13285 Marseille Cedex 2, France **/Treatment of depressive conditions in the elderly./** La therapeutique des etats depressifs du sujet age. Revue de Geriatrie. 5(3):121-122, 1980.

Treatment for depression in elderly subjects is examined. The various therapeutic means used to treat this disorder include: antidepressant drugs, anxiolytic drugs, electroshock therapy, and psychotherapy. Certain aspects in the treatment of the elderly which a physician must be aware of are: the need to maintain an effective dose until improvement is demonstrated, the need to prescribe progressive doses adapted to the somatic context, and the need to discontinue treatment gradually. Even though relatively small doses of medication are often effective, there are cases of heavy melancholic conditions when higher doses or electroshock therapy are needed. (Journal abstract modified)

003579 Braestrup, Claus; Nielsen, Mogens. Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Multiple benzodiazepine receptors.** Trends in NeuroSciences. 3(12):301-303, 1980.

Research studies suggesting that more than one type of benzodiazepine (BZ) receptor exists are reviewed. Results incompatible with the presence of a single class of noninteracting BZ receptors were obtained first by Squires in 1979. He found that a new class of agents, the triazolopyridazines, inhibited 3H-diazepam binding with shallow dose response curves, yielding Hill coefficients below unity. Also incompatible with the presence of a single class of BZ receptors with noninteracting sites was the finding of mixed type competitive inhibition of 3H-diazepam and 3H-FNM binding by ethyl beta-carboline-3-carboxylate, which has a very high affinity for BZ receptors. Other topics discussed include: negative cooperativity; the physiology of BZ1 and BZ2 receptors; and direct evidence for multiple receptors. 11 references.

003580 Burian, W.; Jedlicka, S. Anton-Proksch Institut, Wien, Austria **/Dependence on tranquillizers (an overview with case studies)./** Abhangigkeit von Tranquilizern (Eine Ubersicht mit Fallbeispielen). Wiener Zeitschrift fur Suchtforschung. 2:13-17, 1979.

Several cases of dependence on tranquilizers and the associated tranquilizer withdrawal syndromes are discussed. The pertinent literature on addiction to tranquilizers is reviewed. The risks of prolonged use of tranquilizers are summarized, with emphasis on establishment of tolerance and suicide attempts. The use of tranquilizers is seen primarily as a substitute for dependence on barbiturates. (Journal abstract modified)

003581 Chang, Kwen-Jen; Hazum, Eli; Cuatrecasas, Pedro. Dept. of Molecular Biology, Wellcome Research Laboratories, Research Triangle Park, NC 27709 **Multiple opiate receptors.** Trends in NeuroSciences. 3(7):160-162, 1980.

The research literature concerning the issue of whether the complex effects of opioid peptides are mediated by single or multiple types of opiate receptors is reviewed. It is noted that substantial pharmacological and biochemical evidence has been accumulated to support the existence of multiple opiate receptors. At least two types of opiate receptors can be classified and studied in detail using biochemical and pharmacological tools. Although it is generally agreed that morphine (mu) receptors mediate the analgesia of opioids, clarification of the physiological function of the enkephalin (delta) receptors in the CNS, the relationship between these two receptor sites, and their relation to other pharmacological effects is still needed. A more selective agonist or antagonist for morphine and enkephalin receptors may help to resolve these problems. 18 references. (Author abstract modified)

003582 Cohen, Marcia; Amdur, Mark A. no address **Medication groups for psychiatric patients.** American Journal of Nursing. 81(2):343-345, 1981.

The way in which medication groups for psychiatric patients operate and provide assistance to outpatients is addressed. The groups are designed to help clients understand the role that psychotropic medications play in maintaining mental health. A problem-solving, task oriented approach helps clients gain insight into their own feelings about taking medication. The groups meet weekly for an hour for 4 to 6 weeks and are led by the staff psychiatrist and the agency nurse. It has been observed that clients tend to perceive their medications in terms of side-effects rather than therapeutic effects. The leaders provide technical information to demystify the process of medication management. Successful involvement of hard to reach patients is also addressed.

003583 Cole, Jonathan O. no address **Psychopharmacology update.** Lexington, MA, Collamore, 1980. 195 p. $18.95.

Important developments in psychopharmacology of the past 5 years are reviewed and counterbalanced by personal experience. A practical review of lithium therapy indicates its firmly established use for acute mania and for the prevention of recurrent episodes of both mania and depression. Drug treatment of anxiety is examined, and it is stated that the combination of drugs and psychotherapy benefits anxious patients. Attention is given also to beta-blocking agents and to senile dementia. Research is presented on fenfluramine therapy in bipolar manic-depressives who do not respond to lithium and on phenothiazine therapy as a cause of tardive dyskinesia.

003584 Cottraux, Jean. Laboratoire de Psychologie Medicale, Hopital Neurologique, 59, boulevard Pinel, F-69394 Lyon Cedex 3, France **/Psychopharmacology and behavioral therapy./** Psychopharmacologie et therapie comportementale. Psychologie Medicale. 12(11):2357-2360, 1980.

The value of combining behavior therapy and psychopharmacology is discussed. Behavior therapy focuses on developing self-control strategies for patients' maladjusted responses; such therapy is associated with psychopharmacology in complex cases. Research shows the effectiveness of combining behavior therapy and the administration of antidepressant drugs in depressed obsessive-compulsive patients, and possibly in agoraphobics; schizophrenic patients could benefit from an association of behavior therapy and neuroleptic drug treatment. Cognitive therapy yields better outcomes than do antidepressant drugs in reactive depression. Biofeedback reduces or stops medication intake in some cases of stress related disorders. The importance of single case designs as alternatives to group designs is emphasized. 8 references. (Journal abstract modified)

003585 Creese, Ian; Sibley, David R. Dept. of Neurosciences, University of California, San Diego, School of Medicine, La Jolla, CA 92093 **Receptor adaptations to centrally acting drugs.** Annual Review of Pharmacology and Toxicology. 21:357-391, 1981.

Studies of CNS drug receptors identified by radioligand binding techniques and the influences of chronic drug treatments upon their number and affinity are reviewed. Cautions in interpreting this research literature are discussed, and studies of alpha-adrenergic, beta-adrenerigc, dopamine, serotonin, muscarinic acetylcholine, GABA, benzodiazepine, an opiate/endorphin receptors are described. It is noted that the molecular mechanisms responsible for the varied receptor changes reported in the literature have yet to be elucidated. It is suggested that the biochemical mechanisms responsible for receptor regulation in the CNS are not unlike those in the periphery. 235 references.

003586 Dorsey, Richard. Otto C. Epp Memorial Hospital, Cincinnati, OH **/Guidelines employed by the Food and Drug Administration in drug scheduling./** Discussion of presentation by Dr. Kartzinel. Psychopharmacology Bulletin. 17(1):42, 1981.

Implications of the criteria used by the U.S. Food and Drug Administration (FDA) in their scheduling of drugs under the Comprehensive Drug Abuse Prevention and Control Act of 1970, are discussed. It is contended that the FDA reached the correct conclusion in deciding that suicidal use per se is not sufficient to establish high abuse potential. However, FDA's proposed action on the amphetamines represents an unsound decision and extremely dubious principles. The FDA's deletion of an indication for a drug which is in fact safe and effective when used as labeled is of doubtful legality. It is urged that the American College of Neuropsychopharmacology oppose FDA's efforts to establish itself as an arbitor of medical practice through the use of labeling and production quotas. (Author abstract modified)

003587 Evans, R. H.; Watkins, J. C. Dept. of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **Pharmacological antagonists of excitant amino acid action.** Life Sciences. 28(12):1303-1308, 1981.

Research studies of pharmacological antagonists of excitant amino acid action are reviewed. Pharmacological receptors for excitant amino acids have been classified into three major types found within the vertebrate CNS. The three types of receptor are exemplified by the action of the selective agonists N-methyl-D-aspartate (NMDA), kainate, and quisqualate. Several compounds have been discovered which are selective antagonists of NMDA evoked excitations, the most potent to date being 2-amino-5-phosphonovalerate (APV). Depression of synaptic excitation by NMDA receptor antagonists indicates a physiological role of these receptors in various regions of the CNS. Potent and selective antagonists for kainate or quisqualate receptors have yet to be developed. However, glutamate diethyl ester (GDEE) and gamma-D-glutamylglycine (DGG), applied microelectrophoretically, selectively depress quisqualate and kainate evoked responses, respectively. Cis-2,3-piperidine dicarboxylate (PDA) and 2-amino-4-phosphonobutyrate (APB) are relatively nonselective antagonists of the three types of excitant receptor. Depression of APV resistant spinal transmissin by PDA and synaptically localized kainate binding in the hippocampus suggest that kainate and/or quisqualate receptors are also involved in excitatory transmission. 67 references. (Author abstract modified)

003588 Ferreri, M. Dept. de Psychiatrie et de Psychologie medicale, Hopital Saint-Antoine, 184, rue du Faubourg-Saint-Antoine, F-75012 Paris, France /**Modern aspects of psychopharmacology.**/ Les donnees modernes de la psychopharmacologie. Evolution Psychiatrique. 45(4):723-749, 1980.

Cerebral neurotransmission and modern psychopharmacology are examined. To date, seven neurotransmitters located at the synapse have been identified, and two types of receptors have been determined. Synaptic transmissions differ according to whether they are aminergic, noradrenergic, etc. Several mechanisms of neurotransmission across a synapse are illustrated. The neuronal system is a major element determining cerebral functioning. Modern psychopharmacology has hypothesized that psychic troubles are based on monoaminic dysfunctions and that schizophrenia results from dopaminergic overactivity. However, the interrelations between all these cerebral functions still remain an enigma. 11 references.

003589 Fidell, Linda S. California State University, Northridge, CA 91330 **Sex differences in psychotropic drug use.** Professional Psychology. 12(1):156-162, 1981.

The relationship between sex differences and the extent, origin, and persistence of psychotropic drug use, particularly the minor and major tranquilizers and stimulants, is explored. Prescription use of psychotropic drugs is extensive, involving millions of persons, mostly women, each year. Consequences of misuse/abuse of psychotropics include: failure to solve underlying problems, psychological dependence, and suicide. Origins of use include greater stress among women, tendency by women to report more numerous mental health symptoms, physician attitudes toward women, and the interaction between symptom presentation and physican expectations. Drug use persists because of low self-esteem, growing acceptance of chemical intervention, failure to recognize some prescription use as abuse, and the dependence component of sex-role stereotypes. Responsibilities of professional psychiatrists are discussed. 17 references. (Author abstract modified)

003590 Fisher, Seymour; Mansbridge, Bruce. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch at Galveston, Galveston, TX **Public judgments on the importance of valium information.** Psychopharmacology Bulletin. 17(1):134, 1981.

Public judgments on the importance of various aspects of information concerning valium were solicited and compared with similar judgments by health professionals. Using a modified Q-sort technique, 86 adult general hospital outpatients selected facts they considered most important for patients to know about valium from a larger group of valium facts. Comparison of these patients judged important facts with information provided in a patient package insert for valium constructed by health professional indicated a generally high degree of concordance between public and expert judgments. The patients were particularly concerned with contraindications, cautions, and complications of the medication.

003591 Forino, Vittorio. Istituto Psichiatrico Italy /**Drug dependence: reflections on and analysis of an experience in the province of Riggio Emilia.**/ Tossicodipendenze: riflessioni e sintesi di una esperienza nella provincia di Reggio Emilia. Rivista Sperimentale di Freniatria. 103(6):1847-1862, 1979.

The effects of new legislation on drug addiction in the province of Reggio Emilia are examined. The new law regulates the use and sale of narcotics and psychotropic substances. Although new legislation is much stricter than was previously true, use is still quite high due to the prescription of barbiturates and antianxiety and antidepressant drugs. Psychoanalysis provides etiologic parameters for addiction among children, adolescents, and adults (personality factors and psychopathologies). Various models of intervention and rehabilitation programs for drug addicts are described. Medical treatment includes the use of agonists, partial antagonists, and antagonists.

003592 Gallagher, Rollin M., III; Chapman, Robert J. Dept. of Psychiatry, University of Vermont, Burlington, VT 05405 **The medication seminar and primary care education.** General Hospital Psychiatry. 3(1):16-23, 1981.

A continuing education seminar on psychotropic medication for primary care physicians and psychiatric trainees in primary care is described. The 12 session course was given at Dartmouth-Hitchcock Medical Center in Hanover, New Hampshire, over a 6 month period. The seminar was designed to emphasize experiential and two way learning. The course objectives included: 1) increasing knowledge about the use of psychotropic medication; 2) decreasing feelings of fear and inadequacy in dealing with psychiatric patients; 3) familiarizing local practitioners with mental health resources; and 4) bridging the traditional gulf between psychiatry and the general physician. An evaluation of the seminar indicated its effectiveness. It is concluded that the impact on the instructors and participants has implications for the design and development of future educational programs in both psychiatry and primary care. 14 references.

003593 Gillis, John S.; Moran, Thomas J. Oregon State University, Corvallis, OR 97331 **An analysis of drug decisions in a state psychiatric hospital.** Journal of Clinical Psychology. 37(1):32-42, 1981.

In an examination of psychoactive drug decision-making, 16 staff physicians at a state psychiatric hospital were asked to make decisions that concerned appropriate medication of 40 hypothetical cases of varying diagnoses. A profile presented for each case described the patient's status on eight symptom dimensions. The physician judges examined each profile and specified appropriate drugs and dose levels for the case. Agreement among judges and their prescriptive policies were studied, as was the manner in which symptoms were weighted in specific drug decisions. While agreement was above chance levels, it was generally very low. Differences in prescriptive choice were traceable to inconsistency in the use of symptom information and individual variations in prescriptive policies because cue (symptom) weighting strategies of judges were dissimilar and sometimes contradictory. 8 references. (Author abstract modified)

003594 Gorodetzky, Charles W. NIDAA Research Center, Lexington, KY **Use of currently available data sources to assess drug scheduling.** Psychopharmacology Bulletin. 17(1):38-40, 1981.

Current and potential sources of data for use in scheduling of available drugs by the Food and Drug Administration Drug Abuse Advisory Committee are reviewed. Recommendations of a subcommittee charged with determining the most rational approach to evaluate the effects of drug scheduling are presented. Major areas to consider in evaluation of effects of drug scheduling include: 1) number of fatal medical problems associated with the use of a drug; 2) number of acute, nonfatal medical problems associated with the use of a drug; 3) availability of drug on the street; 4) legitimate medical use; and 5) diversion and illegal manufacture. (Author abstract modified)

003595 Grunbaum, Adolf. Dept. of Philosophy, University of Pittsburgh, Pittsburgh, PA 15260 **The placebo concept.** Behaviour Research and Therapy. 19(2):157-167, 1981.

The placebo concept is examined and analyzed in terms of A. K. Shapiro's influential definition of placebo. It is argued that throughout the medical, psychological, and psychiatric literature, the terminology used to characterize placebo is misleading, imprecise, and conducive to conceptual confusion in research on their effects. A precise new vocabulary is proposed to supplant the traditional language in which the results of placebo research are usually couched. Shapiro's construct of the generic placebo is based on objective rather than dependent or therapeutic beliefs. 23 references. (Author abstract modified)

003596 Guelfi, J. D. Clinique des Maladies Mentales et de l'Encephale, 100, rue de la Sante, F-75674 Paris Cedex, France / **Practical implications of modern psychopharmacological data.**/ Implications pratiques des donnees modernes de la psychopharmacologie. Evolution Psychiatrique. 45(4):805-823, 1980.

Recent knowledge in psychopharmacology is reviewed. Results of research on the pharmacokinetics of psychotropic drugs are somewhat ambiguous; however, the therapist, when prescribing them, is advised to use a rational approach. The importance of measuring plasma levels of antidepressants, of considering their combinability, and of understanding lithium sensitivity better is emphasized. Research into new antidepressant molecules has dealt mainly with biogenic amine precursors and with molecules having a specific action on serotonin, noradrenaline, dopamine, and certain hormonal substances. Plasma levels of neuroleptics and molecules having specific action are also being researched. Pharmacokinetic studies of benzodiazepines should lead to better indications for their use. The role of beta-blocking drugs in the pathology of anxiety with somatic manifestation is also mentioned. 94 references. (Journal abstract modified)

003597 Harrer, G. Institut fur forensische Psychiatrie, Universitat Salzburg, Ignaz-Harrer-Str. 79, A-5020 Salzburg, Austria / **The use of antidepressants in psychiatry.**/ Antidepressiva in der Praxis. Psycho. 6(8):388, 391-392, 394, 1980.

The different possibilities for the use of antidepressant drugs in endogenous and psychogenic depressions are discussed. Based on the assumption that in endogenous depression the sensitivity of postsynaptic receptors is reduced and that in psychogenic depression there is a depletion of biogenic amines on account of stress, antidepressants seem to be valuable in the treatment of these forms of depression. The supply of antidepressants has increased dramatically through the years. Choosing the right drug means knowing the exact state of psychopathologic symptoms. New possibilities of treating patients resistant to antidepressant therapy are also pointed out. 8 references. (Journal abstract modified)

003598 Heiman, Elliott M.; Wood, Gay. Dept. of Psychiatry, College of Medicine, University of Arizona, Tucson, AZ 85724 **Patient characteristics and clinician attitudes influencing the prescribing of benzodiazepines.** Journal of Clinical Psychiatry. 42(2):71-73, 1981.

A questionnaire, designed to evaluate the effect of patient characteristics and clinical attitudes on the prescribing of benzodiazepines was distributed to 86 members of the departments of psychiatry and family practice. The return rate was 87%. Of the respondents, 30% were consistently for, 20% were consistently against, and 50% were neither for nor against the use of benzodiazepines. Prescribing decisions apparently depended on a complex interaction of patient sex, employment, symptom severity, and chronicity, and the respondent's attitudes about the drugs. Plans are under way to revise the questionnaire, undertake in-depth interviews, and compare questionnaire data with actual prescribing practice. 10 references. (Author abstract)

003599 Hemminki, Elina. Psykofarmakaprojekti, Alkoholitutkimussaatio, Kalevankatu 12, SF-00100 Helsinki 10, Finland **Quality of reports of clinical trials submitted by the dr industry to the Finnish and Swedish control authorities.** Euro Journal of Clinical Pharmacology. 19(3):157-165, 1981.

The quality of trials used in support of applications to the Finnish and Swedish control authorities for licensing drugs was examined. All applications for psychotropic drugs received by Finnish and Swedish drug control authorities in the years 1965, 1970, 1974, and 1975 were studied. In addition, a random sample of applications for other drugs was selected in Finland. All reports of clinical trials on the therapeutic efficacy of the drugs were included. Many trials were uncontrolled, and in controlled trials, major drawbacks in the quality of the trial design and in the accuracy of reporting were often found. The number of patients in each controlled trial was small, and the majority of trials concerned selected groups of patients. Measures of effectiveness were often such that it was impossible to establish the overall benefit of the drug. Adverse effects were handled separately and were not adequately combined with efficacy data. 36 references. (Author abstract modified)

003600 Ho, I. K.; Harris, R. Adron. Dept. of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, MS 39216 **Mechanism of action of barbiturates.** Annual Review of Pharmacology and Toxicology. 21:83-111, 1981.

The neurochemical effects of acute and chronic barbiturate administration are reviewed, with emphasis on the relationship between neurochemical changes and the development of tolerance and dependence. In terms of the biochemical event, most investigations of barbiturate intoxication, tolerance, and dependence have been concerned with the role of neurotransmitters. The evidence at present is strongest for GABA involvement in the acute effects of barbiturates and for norepinephrine and GABA involvement in the development of tolerance. Because neurotransmitters, membrane lipids, macromolecules, and ions are intimately related in terms of synaptic transmission, it is concluded that these substances are crucial elements in the mechanisms of barbiturate tolerance and dependence. 203 references.

003601 Holt, John M. Pharmaceutical Division, Eli Lilly and Co., Indianapolis, IN **Impact of drug scheduling on utilization.** Psychopharmacology Bulletin. 17(1):43-44, 1981.

The impact of drug scheduling by the U.S. Food and Drug Administration under the requirements of the Comphrensive Drug Abuse Prevention and Control Act of 1970 on drug utilization and health care costs is described. A hypothetical example of the impact on a drug manufacturer of the rescheduling of one of its products is examined. It is contended that the adoption of controls is a costly exercise. If controls are accompanied by adverse publicity with a consequent shift in utilization to other manufacturers' pharmeceuticals, increasing expenditures will occur for product lines with decreased volume to offset costs. 6 references. (Author abstract modified)

003602 Hughes, Richard; Brewin, Robert. no address **The tranquilizing of America.** New York, Harcourt Brace Jovanovich, 1979. 325 p. $11.95.

The abuse of tranquilizers and other prescription drugs by persons who do not consider themselves drug abusers is examined as a major American health problem. It is suggested that doctors and drug companies may be held responsible. The overuse of such drugs as Valium by doctors who think they are giving their patients the relief they seek is documented. The use of drugs for hyperactivity and the tranquilizing of the aged are discussed. Over the counter drugs which satisfy the tranquilizing needs of the nation are considered. It is concluded that in America the strength of the individual is being swept aside in a heedless rush for the quick and easy chemical way out. (Journal abstract modified)

003603 Janowsky, Esther C.; Risch, Craig; Janowsky, David S. Janowsky, D.: University of California, San Diego, School of Medicine, M-003, La Jolla, CA 92093 **Effects of anesthesia on patients taking psychotropic drugs.** Journal of Clinical Psychopharmacology. 1(1):14-20, 1981.

The effects of anesthesia on patients taking antipsychotic drugs, tricyclic antidepressants, monoamine oxidase inhibitors, and lithium carbonate are reviewed. Since psychotropic drugs generally exert profound effects on central and periphral neurotransmitter and ionic mechanisms, prior intake of these drugs is an important consideration in the management of the patient about to undergo anesthesia and surgery. Topics reviewed include: effects of phenothiazine, thioxanthenes, and butyrophenones on narcotic analgesics; their interactions with CNS depressants such as sedative/hypnotics and barbiturates; sympathomimetic drug interactions; anticholinergic drug interactions; interactions with inhalation anesthetics; interactions with conduction anesthesia; and vasopressor, anticholinergic, and barbiturate/sedative hypnotic interactions with tricyclic antidepressants; monoamine oxidase inhibitor interactions with sympathetic amines; narcotic analgesics, sedative/hypnotic barbiturates, and muscle relaxants; and lithium carbonate interactions with muscle relaxants and barbiturates. 81 references. (Author abstract modified)

003604 Jeanneau, A. 19, La Roseraie, 108, avenue de Paris, F-78000 Versailles, France /**Psychiatric movements and psychopharmacology: between affect and representation.**/ Mouvements psychiatriques et psychopharmacologie: entre l'affect et la representation. Evolution Psychiatrique. 45(4):691-703, 1980.

Psychotropic drugs are discussed in light of Freudian metapsychology. A psychotropic drug causes an artificial weakening of instinctive affective forces. If impulses can be viewed as being composed of a representation and an affect, then the chemical has an impact on the level of the affect. It is proposed that this theoretical basis also applies to daily reality. The doctor-patient relationship during psychopharmacological treatment is discussed, and the bases of psychoanalytical therapy are reviewed. 20 references. (Journal abstract modified)

003605 Karlov, V. A. no address /**Questions of differentiated treatment for epileptic patients.**/ Voprosy differentsirovannogo lecheniya bol'nykh epilepsiyey Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(6):863-867, 1980.

A program of differentiated treatment was carried out on a group of 286 severely afflicted epileptic patients, 102 of whom subsequently achieved cessation or significant reduction of paroxysms. A number of current problems in epileptic therapy are discussed, including: the pharmacodynamics and pharmacokinetics of antiepileptic drugs and their proper dosages; the interval between dosages; the interaction of antiepileptic drugs with other types of drugs; combined medication; specification of the characteristics of petit mal seizures in order to facilitate individualization of treatment; the role of sleep in epileptic therapy; and the concomitance of epilepsy and hyposomnia. 20 references. (Journal abstract modified)

003606 Kartzinel, Ronald. Food and Drug Administration, Rockville, MD **Guidelines for scheduling drugs under the Controlled Substances Act.** Psychopharmacology Bulletin. 17(1):40-42, 1981.

Five of the most recent scheduling recommendations made by the U.S. Food and Drug Administration (FDA) under the Comprehensive Drug Abuse Prevention and Control Act of 1970 (concerning pentazocine, phencyclidine, marihuana, propoxyphene, and amphetamines) are reviewed. It is noted that under the Act, three criteria are examined (potential for abuse, accepted medical use, and dependence) in determining the place of a substance on the schedule. (Author abstract modified)

003607 Kessler, Kenneth A.; Waletzky, Jeremy P. 2020 K St., NW, Suite 810, Washington, DC 20006 **Clinical use of the antipsychotics.** American Journal of Psychiatry. 138(2):202-209, 1981.

Current practical information on the clinical management of acute episodes and maintenance therapy in schizophrenia, including dosage schedules, plasma level determinations, and side-effects (tardive dyskinesia and reversible extrapyramidal syndromes), is reviewed. All neuroleptics given in equivalent doses produce about the same degree of antipsychotic activity. The most common cause of treatment failure in acute psychosis is an inadequate dose, and the most common cause of relapse is patient noncompliance. It is concluded that maintenance medication should be given at the lowest dose that will sustain improvement. Several new alternative drug treatments are also discussed. 68 references. (Author abstract modified)

003608 Kline, Nathan S.; Angst, Jules. Dept. of Psychiatry, Columbia University, New York, NY 10027 **Psychiatric syndromes and drug treatment.** New York, Jason Aronson, 1979. 304 p.

A clear, systematic approach to decision-making regarding the administration of psychotropic drugs to individual patients, which is based on a classification by syndromes, is presented. The grouping of patients for the purpose of choice, dosage, and administration of medications is based on controlled studies and reported clinical experience. General principles of psychopharmacological treatment are presented, the syndromes and their psychopathology and pharmacological treatment are delineated, short summaries of the psychopharmaceuticals (action, dosage, indication, contraindication) are given, side-effects are discussed, and long-term management and prophylaxis are reviewed. 241 references.

003609 Lambert, P. A. Centre Hospitalier Specialise de Bassens, Clinique de Bressieux, F-73011 Chambery Cedex, France / **The history of psychotropic drugs.**/ Histoire des psychotropes. Evolution Psychiatrique. 45(4):669-689, 1980.

The history of psychotropic drugs is reviewed. Narcotic and hallucinogenic plants have been known and used by man since ancient times, but Lewin first described and classified these substances in 1927. The modern period of psychotropic drugs is said to date from 1952, when chlorpromazine was discovered and when it was learned that psychotropic drugs could be used in treating chronic mental disorders (by exciting, calming, or disturbing psychic functions). Neuroleptics are used to treat schizophrenia; tricyclics and monoamine oxidase inhibitors have antidepressant properties; and lithium and dipropylacetamide are mood stabilizers. Recent research has led to the production of additional drugs, and psychopharmacological research now occupies second place in the medical field, after research on cardiovascular illness. 46 references. (Journal abstract modified)

003610 Langer, S. Z.; Briley, M. Synthelabo L.E.R.S., 58, rue de la Glaciere, F-75013 Paris, France **High-affinity 3H-imipramine binding: a new biological tool for studies in depression.** Trends in NeuroSciences. 4(2):28-31, 1981.

The existing data on the high affinity tricyclic antidepressant binding site is reviewed, and the suggestion that 3H-imipramine binding is a useful tool in biological psychiatry is offered. Topics discussed include: high affinity 3H-imipramine binding sites in the brain; effects of various chronic treatments on 3H-imipramine binding; presence of high affinity 3H-imipramine binding sites in human platelets; and the possible significance and research potential of 3H-imipramine binding. It is concluded that the data obtained for 3H-imipramine binding studies are consistent with the indoleamine hypothesis of depression, which implicates changes in serotonin neurotransmission in the pathogenesis of depression. The utility of 3H-imipramine binding studies in the investigation of the biological basis of depression is noted. 16 references.

003611 Lewis, John William; Rance, Michael John. Reckitt and Colman, Pharmaceutical Division, Dansom Lane, Hull, England **Structure activity and receptor binding of antagonist analgesics.** Psychopharmacology Bulletin. 17(1):83-85, 1981.

The structure activity and receptor binding of antagonist analgesics are reviewed, and the relationship between analgesic effects and manifestations of physical dependence is discussed. Apart from the N-substituent, several other structural features have been identified as being of particular importance in conferring morphine antagonist character; most important is the presence of a phenolic hydroxyl group. In the whole range of opioids having mixed agonist/antagonist actions, it has been shown that there are qualitative differences which can only be explained by the existence of the multiple opioid receptors. It is noted that the receptor kinetics of buprenorphine and its mu partial agonist profile combine to produce a situation in which substantial, true, morphinomimetic activity is separated from the major manifestations of physical dependence to yield an effective long-lasting analgesic with a limited abuse potential. 13 references. (Author abstract modified)

003612 Linde, O. K. Pfalzklinik Landeck, D-6749 Klingenmunster, West Germany **/Neuroleptics: interactions with food -- chemical and pharmacodynamic studies on the interactions of coffee and tea./** Neuroleptika: interaktionen mit Nahrungsmitteln -- chemische und pharmakodynamische Untersuchungen zur Interaktion von Kaffe- und Teeinfusen. Psycho. 6(8):420, 1980.

A study by Kulhanek, Linde, Meisenberg, and Parish on the interaction of the effects of coffee and tea in psychiatric patients is discussed. In addition to the known effects of caffeine as an antiparkinsonian remedy, the interaction of tannic acid with caffeine produces alkaloids and therefore reduces caffeine absorption. This explains why large amounts of coffee and tea can be consumed by psychiatric patients without the expected stimulative effects.

003613 Lipton, S. no address **Relief of pain in clinical practice.** Oxford, England, Blackwell Scientific Publications, 1979. 373 p. L18.00.

A summary of the clinical experiences of a leading pain relief physician is presented. Topics discussed include: basic pain relief treatment; relevant anatomy and physiology of pain; pain in the head, neck and upper limb; the intervertebral disc; treatment of cancer pain; postherpetic neuralgia; pain relief via electric stimulation, acupuncture, and nerve blocks; and theories of pain.

003614 Maher, Jane. Meyerstein Institute of Radiotherapy and Oncology, Middlesex Hospital, London W1P 7PN, England **Intravenous lorazepam to prevent nausea and vomiting associated with cancer chemotherapy.** Lancet. No. 8211:91-92, 1981.

The efficacy of using intravenous lorazepam with cancer patients to prevent nausea and vomiting associated with chemotherapy is noted. Vomiting in some cases occurs like a conditioned reflex with each injection and may begin before chemotherapy is given and continue for several hours afterwards. Once such a pattern is established conventional antiemetics, even combined with phenothiazines, have little impact unless heavy sedation is given. Evidence is cited that indicates that injection of lorazepam before chemotherapy combined with standard, centrally acting antiemetics is a safe and useful way of improving toleration of chemotherapy. Seven patients were studied for at least three courses of multiple drug chemotherapy given 3 to 4 weeks apart. 5 references.

003615 Martin, I. L. Neurochemical Pharmacology Unit, Medical Research Council Centre, Medical School, Hills Road, Cambridge CB2 2QH, England **Endogenous ligands for benzodiazepine receptors.** Trends in NeuroSciences. 3(12):299-301, 1980.

Research attempts to identify a naturally occurring compound in the brain which normally interacts with the benzodiazepine receptor are reviewed. The benzodiazepines currently available to the clinician show a broad spectrum of activity; it has not been possible to differentiate the pharmacological profile of any member of the class from those of its cogeners. The classical 1,4-benzodiazepines appear to have the same affinity for the different subpopulations of the benzodiazepine receptors that are known to exist. The multiplicity of receptors may well imply that individual subpopulations mediate different pharmacological effects. The natural ligands for these receptors have yet to be identified, but hold much promise for the clinical pharmacologist in his attempts to develop novel compounds with a more restricted and useful spectrum of activity. 8 references.

003616 Morselli, Paolo L. L.E.R.S.-Synthelabo, 58, rue de la Glaciere, F-75621 Paris Cedex 13, France **/The use of pharmacokinetics in the followup of psychiatric patients./** Apport de la pharmacocinetique au suivi des malades psychiatriques. Evolution Psychiatrique. 45(4):751-759, 1980.

The use of pharmacokinetics in establishing a psychiatric therapy is discussed. It has been argued that pharmacokinetics has no practical application, but this is true only if a laboratory study alone is considered. However, if employed in a clinical setting, pharmacokinetics can have practical applications. Such a study would involve establishing a pharmacokinetic profile, verifying this profile in each patient, and determining the therapeutic and toxic thresholds as well as the possible interactions. It is recommended that biological monitoring of each patient, including monitoring of plasma levels, also should be undertaken. It is thought that such an approach can be quite useful in establishing a therapeutic schema. 26 references.

003617 no author. no address **Abstracts of the Annual General Conference of the European Brain and Behaviour Society, held at Louvain-la-Neuve, Belgium, on November 13-15th, 1980.** Behavioural Brain Research. 2(2):237-289, 1981.

Summaries of 48 papers read at the Annual General Conference of the European Brain and Behaviour Society, held at Louvain-la-Neuve, Belgium, in November, 1980 are presented. Topics discussed include: alpha-striation, a spatial periodicity appearing in stroboscopically illuminated moving random dot patterns; delayed matching to sample in rats; retinal input to the nucleus of the optic tract; neuronal consequences of imprinting; perceptual learning in a grating discrimination task; visual attention; perceptual hemisphere asymmetries; circadian changes in photic responses; effects of morphine on learning; human proprioception under stroboscopic illumination; piracetam and learning; optokinetic nystagmus; eye/hand coordination in children; visuomotor behavior of callosum sectioned rats; scent marking and dominance in gerbils; effects of rearing conditions on neural development; vasopressin effects on learning; hormonal control of animal sexual behavior; chronic amphetamine and latent inhibition; and pattern discrimination in binocularly deprived cats.

003618 Norell, Staffan E. Depts. of Social Medicine and Ophthalamology, Karolinska Institutet, Huddinge University Hospital, Huddinge, Sweden **Accuracy of patient interviews and estimates by clinical staff in determining medication compliance.** Social Science & Medicine. 15E(1):57-61, 1981.

The accuracy of patient interviews and estimates by clinical staff in determining medication compliance among patients treated with pilocarpine to prevent visual loss from glaucoma was investigated. Objective and detailed information on self-medication behavior was obtained using a recording medication monitor. Results indicated that estimates by clinical staff were not useful in determining compliance. Patient interviews identified seven of 16 patients who missed doses at least once a week. However, underreporting of missed doses was a major problem in determining compliance by interview. Of 73 patients interviewed, only 4% reported two or more missed doses during the past 7 days, whereas monitor records showed that 33% of the Ss missed at least two doses, and that 16% missed at least six doses during the past week. 28 references. (Author abstract modified)

003619 Noyes, Russell, Jr. Dept. of Psychiatry, University of Iowa, 500 Newton Rd., Iowa City, IA 52242 **Treatment of cancer pain.** Psychosomatic Medicine. 43(1):57-70, 1981.

Treatment of cancer pain is discussed with emphasis on the psychological aspects of cancer pain and the place of certain psychological techniques and psychotropic drugs in a comprehensive treatment plan. Undertreatment of cancer pain often results both from the limited expectations of patients and from the inadequate knowledge of physicians. When indicated, analgesic drugs should be administered according to a regular schedule and in sufficient dose to prevent the emergence of pain. Psychological techniques including supportive psychotherapy, relaxation training, hypnosis, and the hospice milieu may contribute to a comprehensive approach to pain. Likewise, psychotropic drugs including phenothiazine and tricyclic antidepressants may be useful adjuncts when administered along with appropriate analgesic medication. Although most pain associated with advanced cancer may be relieved by currently available methods, research in this area is urgently needed. 71 references. (Author abstract modified)

003620 Palfreyman, Michael G.; Schechter, Paul J.; Buckett, William R.; Tell, Guy P.; Koch-Weser, Jan. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg-Cedex, France **The pharmacology of GABA-transaminase inhibitors.** Biochemical Pharmacology. 30(8):817-824, 1981.

The pharmacology of GABA-transaminase (GABA-T) inhibitors is reviewed, and the clinical utility of these agents is evaluated. Topics discussed include: pharmacological effect of GABA-T inhibitors; sedation, hypothermia, and antinociceptive action; anticonvulsant effects; dyskinetic effects of intracerebral injections; antianxiety effects; effect on dopaminergic pathways; animal models of Huntington's disease; and clinical studies with GABA-T inhibitors. It is concluded that a well tolerated GABA-T inhibitor which produces the desired neurochemical change will be useful to explore the role of GABA in normal CNS function and in the pathogenesis of some disease states. 107 references.

003621 Park, B. K.; Breckenridge, A. M. Dept. of Pharmacology and Therapeutics, University of Liverpool, P.O. Box 147, Liverpool, L693BX, England **Clinical implications of enzyme induction and enzyme inhibition.** Clinical Pharmacokinetics. 6(1):1-24, 1981.

The research literature concerning modulation of the activity of drug metabolizing enzymes by enzyme induction and enzyme inhibition is reviewed, and the biochemical, clinical, and toxicological consequences of these phenomena are discussed. Drugs most frequently encountered as enzyme inducing agents in man are barbiturates, rifampicin, and phenytoin. Enhancement of drug metabolism by ethanol, tobacco smoking, and diet may also involve enzyme induction. Enzyme induction has been assessed in man by measuring changes in the pharmacokinetics of a marker drug, or changes in the disposition of endogenous compounds, such as gamma-glutamyltranspeptidase, D-glucaric acid, and 6beta-hydroxycortisol. The effect on the rate of elimination of a particular drug due to enzyme inhibition will depend upon the fraction of the dose that is normally metabolized by the inhibited enzyme and on the affinity of the enzyme for the drug and the inhibitor. 175 references. (Author abstract modified)

003622 Perucca, Emilio. Clinical Pharmacology Unit, Institute of Neurology, National Hospital, Queen Square, London WC1N 3BG, England **Drug interactions in epilepsy.** Arquivos de Neuro-Psiquiatria. 38(4):331-340, 1980.

The clinical consequence of interactions between antiepileptic drugs are discussed, with emphasis on the fact that the physician should consider carefully the need for and implications of adding a new compound to any therapeutic regime. The physician should be prepared for the possibility of an interaction whenever an unusual response in noted. Serum drug levels are seen as a valuable tool in recognizing and managing most types of interactions, but in no case can they be a substitute for careful observations and evaluation of the patient's symptoms and physical findings. 12 references. (Author abstract modified)

003623 Raskin, Neil H. Dept. of Neurology, University of California School of Medicine, San Francisco, CA 94143 **Pharmacology of migraine.** Annual Review of Pharmacology and Toxicology. 21:463-478, 1981.

The pharmacology of migraine is reviewed, and evidence supporting the hypothesis that migraine is a disorder of the CNS is evaluated. The role of the following drugs in altering the neurotransmitter function of serotonin is examined: extracranial vasoconstrictors (erogotamine, dihydroergotamine, and caffeine); the serotonin antagonists (methysergide and cyproheptadine), and beta-adrenergic blocker (propranolol); a tricyclic antidepressant (amitriptyline), a monoamine oxidase inhibitor (phenelzine); and a vasodilator (papaverine). The most persuasive of the several lines of evidence which suggest that migraine is a CNS disorder is the common mode of action of the antimigrainous drugs in the suppression of the firing rate of brainstem serotonergic neurons. It is suggested that the cardinal abnormality of migraine is that the modulation of serotonin release is defective, leading to sporadically low synaptic serotonin levels and secondarily increased raphe neuronal firing rates. 119 references.

003624 Reed, John P., Jr. Southern Baptist Theological Seminary, 2825 Lexington Rd., Louisville, KY 40206 **Mind/brain in the age of psychopharmacology: a crossroads for medicine and ministry.** Journal of Pastoral Care. 35(1):3-17, 1981.

The implications of the tacit scientific reductionism which underlies the psychopharmacological movement in psychiatry for the practice of psychiatry and the ministry are discussed. These advances in understanding brain chemistry point to an organic basis of mental disorder. The integration of brain chemistry with psychology is the principle task facing psychatry and ministry. This interpretive role is different from the diagnostic in that the minister continues to treat mental illness as charged with meaning and symbols and not mere signs of synaptic disruption. Although symptoms can be removed with medication, without the element of self-transcendence wherein the person beholds oneself in one's striving, willing, and purposing, freedom and individuality can be lost. The potential for personalization through the help of certain medications is present. Both physicians and ministers must avoid treating psychopharmacology as the cure all. The medical community stands to gain by the adoption of a broader model, one that treats persons in their totality.

003625 Rifkin, Arthur. Mount Sinai School of Medicine, New York, NY **Chronic drug treatment of the chronically ill: benefits and risks.** Journal of the National Association of Private Psychiatric Hospitals. 11(5):22-26, 1980.

The advantages and disadvantages of long-term drug treatment of schizophrenia and affective disorder are reviewed. The evidence of a number of studies has indicated that long-term use of antipsychotics such as chlorpromazine and fluphenazine prevents relapse or exacerbation in schizophrenics patients. One serious side effect of long-term antipsychotic use is tardive dyskinesia, for which no treatment has been established. Adverse reactions that may mimic psychopathological symptoms include akathisia and akinesia. Such side effects may cause or increase noncompliance, a major cause of drug unresponsiveness among chronic schizophrenics. As for the long-term treatment of affective illness, lithium has been proven to be effective for prophylaxis of bipolar illness and for treatment of bipolar depression, and tricyclic antidepressants are equally effective in the prophylaxis of unipolar depression. The risk of renal toxicity, and the consideration involved in deciding to institute prophylactic treatment for affective disorder are discussed. 12 references.

003626 Rosenbaum, Janet. University of Windsor, School of Nursing, Windsor, Ontario, Canada **Widows and widowers and their medication use: nursing implications.** Journal of Psychiatric Nursing and Mental Health Services. 19(1):17-19, 1981.

Use of psychotropic medication and alcohol and level of depression was examined in a descriptive study of widows and widowers (n=56) belonging to or not belonging to a self-help group. Results show: there was an increase in the use of tranquilizers, hypnotics, and antidepressants following bereavement, which, while decreasing somewhat over time, remained high relative to prebereavement levels; psychotropic medications were most often prescribed by physicians and Ss tended to continue to use them, some for years; medications were most often used to relax or to help with sleep; most Ss reported receiving no or unsatisfactory instructions regarding medications; only 4 of 26 Ss who knew the spouse was dying had open and free discussions about death, and none of those who had discussed death was taking medication following bereavement; Ss reported feeling closest to their children at the time of bereavement; level of depression and use of psychotropics were positively related; and no significant trends in alcohol use were found. Implications for nursing care of the dying patient and the spouse are discussed with reference to assisting them in working through the grieving process. 4 references.

003627 Rossie, George Vincent. Washington State University **Psychoactive medication use and abuse among an adult rural population. (Ph.D. dissertation).** Dissertation Abstracts International. 41(8):3238-B, 1981. Ann Arbor, Univ. Microfilms No. 8104146, 89p., 1980.

A sample of 390 residents of a rural county in eastern Washington completed a multiple wave mail survey assessing their use of psychoactive medications and drugs. Included in the 63 item questionnaire were questions measuring incidence and frequency of the use of over the counter drugs, prescription antianxiety agents, sedative/hypnotics, codeine cough preparations, opiate analgesics, stimulants, psychotropics, alcohol, and marihuana. Data are examined in terms of the pattern and prevalence of psychoactive drug use, the interrelations among stress and health factors and drug and alcohol use, the relationships between drug use and demographic factors and nonproblem behaviors, and the relationships between attitudes and drug use. Results show stress problems to be significantly correlated with the use of all psychoactive substances including alcohol while medical problems were significantly related to the use of all drugs except alcohol and stimulants. Results suggest that the patterns of drug prescriptions and drug use in this rural sample tend to deviate substantially from results obtained in national studies. (Journal abstract modified)

003628 Rouillon, F. Interne des Hopitaux de Paris, 100-102, rue de la Sante, F-75674 Paris Cedex 14, France **/Neuroleptic activity: a summary of Professor Jacques Glowinski's presentation./** Mecanismes d'action des neuroleptiques: compte rendu de la communication du Professeur Jacques Glowinski. Evolution Psychiatrique. 45(4):761-766, 1980.

The discovery of how neuroleptics act and the development of this knowledge to the present are discussed. The dopaminergic activity of neuroleptics was discovered during observation of the cataleptic properties of reserpine. This knowledge was amplified in three stages: Carlsson's discovery of increased dopaminergic activity due to the activation of dopaminergic neurons as a result of a blockage of postsynaptic receptors; Kebabian and Greengard's isolation of adenylcyclase and demonstration of its link to dopamine activated receptors; and Snyder's identification of receptors by fixing on them dopaminergic agonists or radioactive neuroleptics. Present research is concerned with the following areas: long-term neuroleptic treatment; histochemical postmortem studies; and animal research to understand the different dopaminergic systems.

003629 Royer, R. J. Service de Pharmacologie et Toxicologie, C.H.R., Nancy, France **/Interactions between alcohol and medications./** Interreactions entre alcool et medicaments. Revue de l'Alcoolisme. 25:21-28, 1979.

The various ways in which psychopharmaceuticals interact with alcohol are discussed. The mechanisms of absorpotion, distribution, and affinity to certain receptors, and drug metabolism are examined. The interaction of alcohol with neuroleptic drugs, tranquilizers, and tricyclic antidepressants is explained. A wide spectrum of often contradictory findings is offered. Contradictions stem from the impossibility of creating identical conditions for experiments. Independent variables such as age, sex, personality, and physical and mental state are the main reasons why it has been impossibile to determine the exact degree and mode of drug/alcohol interaction. (Journal abstract modified)

003630 Schou, Mogens. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Bibliography on the biology and pharmacology of lithium.** Neuropsychobiology. 7(1):26-55, 1981.

A bibliography covering the period 1978 through 1980 and concerned with the biology and pharmacology of lithium is presented. Included are references to all aspects of the biology, pharmacology, toxicology, and clinical use of lithium with psychiatric patients. Most of the papers listed contain original data; textbooks and congress abstracts are listed only occasionally.

003631 Scott, Clarissa Stewart. University of Miami **The influence of patient beliefs on compliance to therapy for diabetes mellitus. (Ph.D. dissertation).** Dissertation Abstracts International. 41(7):2739-B, 1981. Ann Arbor, Univ. Microfilms No. 8100745, 153p., 1980.

Compliance with an insulin regimen and related beliefs were studied in a sample of adult onset diabetic patients. The 46 Ss were from a low income clinic, and most were female and Black. A comparison of objective measures and self-reports showed that 17% of the sample were not truthful in regard to taking their insulin as directed. Insulin compliant patients were more likely to hold the belief that insulin use was effective in the control of diabetes. This was also true with regard to patients who were compliant with weight loss. It is concluded that noncompliant patients are more likely than compliant patients to believe they should use their own judgment in deciding how much of the doctor's advice to follow. (Journal abstract modified)

003632 Shopsin, Baron. New York University School of Medicine, New York, NY 10016 **Second generation antidepressants: a clinical pharmacotherapeutic research strategy.** Psychopharmacology Bulletin. 17(1):33-35, 1981.

A clinical pharmacotherapeutic research strategy for depressive disorders, consisting of the use of investigational drugs with defined pharmacological and biochemical activity, is described, and results of such studies are discussed. The specific actions of a variety of new and/or investigational antidepressant drugs including their dominant central action on norepinephrine (NE), serotonin (5-HT), or dopamine (DA) are described. It is concluded that efforts to define the specific amine or amines responsible for antidepressant effects of antidepressant drugs appear unrewarding, since any of the amines alone or in combination may be associated with an antidepressant effect of drugs in man. 5 references. (Author abstract modified)

003633 Simon, P.; Frances, H.; Thiebot, M. H.; Puech, A. Dept. de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris Cedex 13, France / **The validity of models in psychopharmacology./** Validite des modeles en psychopharmacologie. Evolution Psychiatrique. 45(4):777-784, 1980.

The use of models in experimental psychopharmacology and the difficulties they present are discussed. Psychopharmacological models are used to discover new medications and, indirectly, to try to understand the mechanisms underlying certain pathological human conditions. To accomplish the first goal, the models must be easy to perform, replicable, specific, and sensitive. The main problems encountered in using such methods are illustrated through four examples: antagonistic effects of reserpine; antagonistic effects of oxotremorine; four plates test; and the heated floor maze. (Journal abstract modified)

003634 Spiker, Duane G. University of Pittsburgh School of Medicine, Pittsburgh, PA **The pharmacological treatment of schizoaffective disorder-depressed: a review of the literature.** Psychopharmacology Bulletin. 17(1):75-78, 1981.

The clinical literature concerning the pharmacological treatment of schizoaffective disorder/depressed patients is reviewed. Studies employing tricyclic antidepressants alone, antipsychotic drugs alone, and antidepressants plus antipsychotics are evaluated. It is concluded that the literature dealing with the pharmacological treatment of schizoaffective disorder/depressed persons is sparse and inconclusive. It is recommended that a good narrative history be taken, with particular emphasis on the chronology of symptoms. Issues concerning diagnosis and nomenclature are noted. 12 references. (Author abstract modified)

003635 Spriet, Alain. Laboratoires Hoechst, Tour Nobel, F-92800 Puteaux, France /**Debate: therapeutic trials in a natural environment./** Debat: les essais therapeutiques dans un environnement naturaliste. Psychologie Medicale. 12(13):2735-2737, 1980.

The advantages and disadvantages of conducting drug trials in a natural environment are discussed. The term natural implies an environment as similar as possible to the everyday environment of the patient, rather than one that represents a hospital setting. It is thought that tests in natural settings will enable physicians to determine more precisely the indications for a particular medication. However, several variables must be considered when evaluating the usefulness of a drug tested in this setting: the doctor-patient relationship; personal events in the life of the patient; the pharmaceutical preparations themselves; and the verification of the treatment. A brief discussion follows the article.

003636 Squire, Larry R.; Davis, Hasker P. V. A. Medical Center, 3350 La Jolla Village Drive, V-116, San Diego, CA 92161 **The pharmacology of memory: a neurobiological perspective.** Annual Review of Pharmacology and Toxicology. 21:323-356, 1981.

Research studies concerning the effects of drugs on memory are summarized in relation to the neurobiology of memory. Six areas of investigation (acetylcholine, protein synthesis, ACTH, vasopressin, opioids, and catecholamines) are considered. In general, the data are consistent with a view of memory whereby information storage occurs as alterations in connectivity along neural pathways already specialized for different kinds of information processing. These intrinsic, information containing neural ensembles are not fully etablished at the moment of learning, but develop and change with time in a way that reflects their modulation by extrinsic systems. The data concerning the putative effects of various drugs on arousal, fear, and attention raise the possibility that modulation reflects specific and different influences on memory, rather than some single influence. 203 references.

003637 Starke, K. Pharmakologisches Institut, Universitat Freiburg, D-7800 Freiburg i. Br., West Germany **Presynaptic receptors.** Annual Review of Pharmacology and Toxicology. 21:7-30, 1981.

Studies concerning the terminology, development, location of receptors, mode of action, and physiological function of presynaptic receptors are reviewed. It is noted that presynaptic receptors, when activated, primarily modify the function of the axon terminals, for instance, transmitter biosynthesis and release. Whether physiologically silent or not, presynaptic receptors may be sites of action of drugs. Imidazoline alpha-adrenoceptor agonists may cause sedation by presynaptic (and soma dendritic) inhibition of central noradrenaline pathways. GABA antagonists may produce convulsions by interrupting GABAergic presynaptic inhibition. Opiates possibly relieve pain because they activate receptors on substance-P terminals. Methylxanthines may stimulate the CNS because they antagonize presynaptic inhibitory effects of adenosine. The diversity of presynaptic receptors as a mechanism for the physiological regulation of neurons is emphasized. 182 references. (Author abstract modified)

003638 Stolberg-Acosta, Robert; Martin-Del-Campo, Enrique. Dept. of Psychiatry, University of Puerto Rico, Medical Sciences Campus, G.P.O. Box 5067, San Juan, Puerto Rico 00936 **What is standard practice in prescribing psychotropics?** Legal Aspects of Medical Practice. 8(3):31-35, 1980.

Justifications for prescribing doses of psychotropic drugs that exceed the recommended dosage of the Physicians' Desk Reference (PDR) are discussed. A survey of antidepressant prescription in 13 community hospitals in greater Philadelphia indicates that in a high percentage of these institutions, the doses often exceeded the maximum recommended in the PDR. This was particularly true for three particular antidepressants, although recommended doses of amitriptyline and imipramine were never overexceeded. Dosage recommendations also were exceeded for the minor tranquilizers. Implications for standard practice are discussed. 23 references.

003639 Tipton, K. F. no address **Neurochemical and biochemical pharmacology.** International review of biochemistry, vol. 26. Lancaster, England, MTP Press, 1979. L15.25.

Six papers on diverse topics in neurochemistry and biochemical pharmacology are presented. Topics discussed include: an overview of cyclic nucleotides and synaptic transmission, including metabolism, factors affecting synthesis and steady-state concentrations in nervous tissue, and synaptic roles for cyclic AMP and cyclic GMP; the storage and secretion of catecholamines; the neurochemistry of the trace amines (meta-tyramine, para-tyramine, beta-phenylethylamine, and tryptamine) in the CNS; histamine function in immune responses, gastric secretion, the cardiovascular system, and the CNS; and the purification, characterization, quantification, localization, and turnover of skeletal muscle acetylcholine receptors.

003640 Tosteson, Daniel C. no address **Lithium and mania.** Scientific American. 244(4):164-166, 168, 171-172,174, 1981.

A review is presented of the relationships among lithium, its movement across membranes, and its use in the treatment of mania. Early research by Cade in the treatment of manic-depressive disorder with lithium salts is reviewed. The similarities among lithium, potassium, and sodium are discussed, as are their more important differences. The structure of cell membranes is delineated, and four types of transport across cell membranes are examined: selective movement of various ions down their respective concentration gradients and electrical potential gradients; pumps, which move ions against concentration and electric potential gradients; exchange diffusion; and cotransport. Research elucidating lithium metabolism in human red blood cells is then summarized, and the movement of lithium across membranes in the individual receiving lithium therapy is outlined in terms of leakage pathways and the lithium-sodium countertransport system. Directions for future research into the lithium ion's mechanism of action in mania and implications for medicine, in general, are discussed.

003641 Val'dman, A. V.; Zvartau, E. E. Institut farmakologii AMN SSSR, Moskva, USSR /**Action on the emotionally reinforced brain system as a means of treating alcoholism and drug addiction pathogenetically.**/ Vozdeystviye na emotsional'nopodkreplyayushchiye sistemy mozga kak sposob patogeneticheskoy terapii alkogolizma i toksikomaniy. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(7):1020-1024, 1980.

The effect of hypothalamic stimulation on emotional reactions to drugs (morphine, cocaine, amphetamines, diazepam and pentobarbital) and alcohol is discussed. Methods for the study and production of effective drugs for prevention and treatment of dependence were developed. Results show that the drugs activate centers of electrical self-stimulation in the brain, an effect which is regarded as basic to the action of the drugs in producing euphoria; and that antieuphoric action is an important consideration in treatment of psychological dependence on narcotic drugs. 16 references. (Journal abstract modified)

003642 Valli, M.; Pringuey, D. Service de Pharmacologie Clinique, C.H.U. de la Timone, F-13385 Marseille Cedex 5, France / **New trends concerning the biochemical mechanism of action of benzodiazepines.**/ Actualites concernant le mecanisme d'action biochimique des benzodiazepines. Therapie. 35(5):561-569, 1980.

Recent research on the biochemical mechanism of benzodiazepines (BZDs) is reviewed. BZDs are widely used in clinical practice as anxiolytics, muscle relaxants, sedatives, and anticonvulsants. Electrophysiological studies have shown a specific interaction of BZD with GABA, an inhibitory neurotransmitter. BZD enhances the physiological effects of GABA. The discovery of saturable and stereospecific binding sites with high affinity for BZD, and their brain distribution indicates a predominantly cortical action of BZD. Furthermore, BZD receptors seem to be linked to GABA receptors and closely connected to the chloride conductance mechanism associated with the GABA receptor. The discovery of BZD receptors suggests the existence of endogenous ligands. Inosine, hypoxanthine or nicotinamide are reported to have BZD like activities, in spite of a relative low affinity for their binding sites. Their putative role as endogenous anxiolytics needs to be supported by behavioral studies. 39 references. (Journal abstract modified)

003643 Vaynshtok, A. B.; Oleynik, L. I. Institut gerontologii, AMN SSSR, Kiev, USSR /**Geriatric aspects of parkinsonism (clinical picture, pathological mechanisms, and multiple treatment).**/ Parkinsonizm v geriatricheskom plane (klinika, patologicheskiye mekhanizmy, kompleksnoye lecheniye). Vestnik Akademii Meditsinskikh Nauk SSSR. No. 12:33-40, 1980.

The clinical picture, pathological mechanisms, and multiple treatment of geriatric parkinsonism were studied in relation to data collected in the course of 12 years on 1,500 elderly patients with parkinsonism, and control groups of healthy people. The processes examined were: catecholamine, mineral, and lipid metabolism, adrenal cortical androgenic and glucocorticoid functions, autoimmune responses, bioelectric activity of muscles, monosynaptic Hoffmann's reflex, and visual evoked potentials. Results show that the age specific changes in the motor sphere during late ontogeny in healthy people have the same direction as in patients with parkinsonism. These changes are more pronounced in patients with parkinsonism. The results show that combined treatment, including the use of drugs affecting the main symptoms of the disease, along with antisclerotic agents and hypotensive drugs, is desirable. 32 references. (Journal abstract modified)

003644 Versiani, Marcio. Instituto Brasileiro de Psiquiatria, Av. Venceslau Bras, 71, 22290 Rio de Janeiro, Brazil /**Therapeutic (III): general characteristics of antipsychotic drugs.**/ Terapeutica (III): antipsicoticos -- principios gerais. Jornal Brasileiro de Psiquiatria. 29(2):87-90, 1980.

General principles of the use of antipsychotic drugs are discussed. Antipsychotics can be divided into three groups according to the different proportion of extrapyramidal, cardiovascular, and anticholinergic side-effects. The clinician should choose a few drugs representative of each group, and should become familiar with their qualities. Treatment should be initiated with small dosages, to be modified later in order to determine the best dosage for the patient. Drug combinations should be avoided. (Journal abstract modified)

003645 Villarreal, Julian E.; Castro, Antonio. Instituto Miles de Terapeutica Experimental, Mexico City, D.F. Mexico **A reformulation of the dual-action model of opioid dependence: opioid-specific neuronal kindling.** Psychopharmacology Bulletin. 17(1):56-58, 1981.

A reformulation is presented of the dual action model of opioid dependence, wherein opioid dependence is attributed to the setting up or sensitizing a kindling mechanism within opioid sensitive neurons. This model of opioid specific kindling can account for abstinence effects seen with antagonist administration during narcotic treatment, termination of chronic narcotic treatement, abstinence like effects produced in dependent monkeys by restraint or by administration of cholinesterase inhibitors, afterdischarges in isolated segments of dependent intestine following single electrical stimuli, abstinence like effects produced by antagonists given months after terminaton of narcotic treatment, and protracted abstinence. It is noted that the chronic activation of the opioid sensitive kindling mechanism results in a progressive buildup of sensitivity to certain triggering stimuli and to an increased capacity of the enkindled structure to discharge, causing overt abstinence like responses of a progressively larger magnitude. 5 references. (Author abstract modified)

003646 Vinar, O. K ovcinu 1519, 182 00 Praha 8, Czechoslovakia **/Psychopharmacology after 20 years of conferences in Jesenik./** Psychofarmakologie po 20 letech konferenci v Jeseniku. Ceskoslovenska Psychiatrie. 75(3):213-222, 1979.

The development of psychopharmacology in the past 20 years in Czechoslovakia is discussed. The report concentrates on the mutual relationship between basic research and clinical practice and on future prospects in the light of psychopharmacology and the pathogenesis of psychoses. Czechoslovakia has specific priorities in the epidemiology of drug use. Anxiolytics more than any other drugs may influence entire social groups. It is concluded that many clinical problems remain unsolved, but impressive improvements have been made in the area of new discoveries in psychopharmacology rather than in the area of therapeutic facilities. 28 references.

003647 Watkins, Gareth; Tarnopolsky, Alex; Jenkins, Linda M. Tarnopolsky. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **Aircraft noise and mental health: II. Use of medicines and health care services.** Psychological Medicine. 11(1):155-168, 1981.

The relationship between aircraft noise from London (Heathrow) Airport, noise annoyance, and the following variables were studied: use of medications, attendance to general practitioners, referrals to outpatient clinics, admission to the hospital, and use of community health or welfare services. Respondents were urban dwellers 16 years old and older. None of the health indicators showed higher uptake in the high noise areas. In areas exposed to high noise the use of nonprescribed drugs was significantly higher among very annoyed than among less annoyed respondents. The use of psychotropic drugs and general practice and inpatient services tended to increase with increasing annoyance both in high noise and low noise areas, but the differences were not significant. Parallels to earlier research are considered. 13 references. (Author abstract modified)

003648 Watkins, J. C.; Evans, R. H. Dept. of Physiology, Medical School, University of Bristol, Bristol BS8 1TD, England **Excitatory amino acid transmitters.** Annual Review of Pharmacology and Toxicology. 21:165-204, 1981.

Research studies of amino acid mediated synaptic excitation utilizing three approaches (development of new agonists and antagonists for determining the pharmacological properties of different excitatory amino acid receptors; use of lesioning techniques to determine the effects of selective neuronal and/or afferent input loss upon regional levels, uptake, and release of suspected transmitters; and study of membrane binding sites for excitatory amino acides by the use of radioactive ligands) are reviewed. The findings of these three lines of research are compared, and gaps in the evidence for amino acid mediated synaptic excitation in specific neuronal pathways are emphasized. It is concluded that knowledge and understanding of this type of central synaptic excitation seems likely to enter a phase of rapid growth. 294 references.

003649 Way, E. Leong. Dept. of Pharmacology, School of Medicine, University of California, San Francisco, CA 94143 / **Recent reviews of biochemical, neurochemical, and pharmacological topics./** Review of reviews. Annual Review of Pharmacology and Toxicology. 21:605-613, 1981.

Recent reviews of selected topics in biochemistry, neurochemistry, and pharmacology are reviewed. Reviews of the following topics are discussed: neuropeptides in the brain; enkephalins and endorphins; tetrodotoxin and saxitoxin; substance-P; presynaptic receptors; radioimmunoassay techniques; male contraceptives; drug dependence; and general pharmacology. The tendency for original research to be presented in proceedings of symposia rather than refereed journals is briefly discussed. 13 references.

003650 Williams, Roger L.; Mamelok, Richard D. Drug Studies Unit, 926 Science, University of California, San Francisco, CA 94143 **Hepatic disease and drug pharmacokinetics.** Clinical Pharmacokinetics. 5(6):528-547, 1980.

Recent research concerning the influence of the liver on drug pharmacokinetics is reviewed, and implications for drug therapy in patients with hepatic disorders are discussed. Studies have confirmed that hepatic disease may alter substantially one or more pharmacokinetic parameters of drug absorption and disposition. Physiological models of hepatic drug elimination have emphasized the importance of physiological variables such as hepatic blood flow, protein binding and intrinsic clearance of the liver on hepatic drug elimination. Both clinical investigations and theoretical considerations have indicated that the influence of hepatic disease on the pharmacokinetics of a drug may be complex and may result in either unchanged, retarded, or even accelerated drug elimination. Changes in response to drugs in patients with hepatic impairment add to this complexity. Although general guidelines may be formulated now to assist clinicians in constructing dosage regimens of several important drug classes (notably the benzodiazepines and barbiturates) in hepatic disease, it is not now possible to predict in an individual the influence of a specific hepatic disease on the disposition of a drug. 88 references. (Author abstract modified)

003651 Wilson, Ronald W.; Elmassian, Bonnie J. Dept. of Natural Science, Michigan State University, East Lansing, MI 48823 **Endorphins.** American Journal of Nursing. 81(4):722-725, 1981.

The use of endorphins and a brief history of their discovery with both human and animal subjects are presented. Endorphins are endogenous compounds with opiate like properties that include the potential to alter pain perception, mood, respiration, and the release of pituitary hormones. Endorphins have been found in the pituitary gland, gastrointestinal tract, and throughout the central nervous system. Chemically, the endorphins are peptides, sequences of several linked amino acids. In addition to research documenting the physiological role of endorphins in the pain process, evidence is reported which implicates these peptides directly or indirectly in various psychoses, in behavioral processes, and in processes of learning. 25 references.

003652 Youdim, M. B. H.; Lovenberg, W.; Sharman, D. F.; Lagnado, J. R. no address **Essays in neurochemistry and neuropharmacology.** Chichester, England, John Wiley, 1980. 282 p. Vol. 4. L19.50.

A collection of papers in neurochemistry and neuropharmacology is presented. Topics discussed include: research concerning biochemical defects or abnormalities in schizophrenia; the molecular processes responsible for release by exocytosis of catecholamines from noradrenergic terminals and from the adrenal medulla; modulation of transmitter release by drugs; the chemistry, kinetics, and possible identity of dopamine-beta-hydroxylase with chromogranin-A; brain enolases; and changes in catecholamine receptor sensitivity.

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Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

003653 Bernier, J. L.; Henichart, J. P.; Warin, V.; Baert, F. INSERM U16, Place de Verdun, F-59045 Lille Cedex, France **Synthesis and structure-activity relationship of a pyrimido(4,5-d)pyrimidine derivative with antidepressant activity.** Journal of Pharmaceutical Sciences. 69(11):1343-1345, 1980.

The synthesis and antidepressant properties of a new pyrimido(4,5-d)pyrimidine are described. Spectral data determined in solution and in the solid state allowed establishment of the relationship between the activity and the conformation of the molecule. The spatial structure seems to be in accordance with a possible binding at the presynaptic alpha-receptor sites. 18 references. (Author abstract)

003654 Bhattacharyya, Pranab K. Quality Control Dept., Hoffman-La Roche Inc., Nutley, NJ 07110 **NMR spectral study of proton transfer in amitriptyline hydrochloride-chlordiazepoxide hydrochloride combinations in dipolar aprotic solvents.** Journal of Pharmaceutical Sciences. 69(2):180-183, 1980.

The singlet resonance due to the two equivalent methyl groups of amitriptyline hydrochloride in dimethyl sulfoxide-d6 solution changed into a doublet with the addition of chlordiazepoxide hydrochloride. A spin decoupling experiment revealed that the doublet originated because of the emergence of observable spin/spin coupling between the tertiary amine proton and the methyl groups. The phenomenon was attributed to the nature of the proton transfer caused by the relative magnitudes of the basicities of the amines in these compounds, which were determined by the inductive and steric effects of the substituents, leading to the formation of hydrogen bonded ion pairs in the aprotic diluent. The enthalpy of the exchange process was 6.4kcal/mole. 11 references. (Author abstract modified)

003655 Blake, James; Chang, Wen-Chang; Li, Choh Hao. Hormone Research Laboratory, 1088 HSW, University of California, San Francisco, CA 94143 **Synthesis and biological activity of human beta-endorphin analogs with disulfide bridges.** International Journal of Peptide Protein Research. 14:275-280, 1979.

Three analogs of human beta-endorphin containing internal cystine bridges were synthesized, and their biological activities were determined. The analogs with disulfide bridges between positions 17 and 26 or 11 and 26 retained full opiate activity (as estimated by guinea-pig ileum assay), whereas the analog with a cystine bridge between positions 7 and 26 showed reduced opiate activity. None of the analogs retained significant immunoactivity as revealed by radioimmunoassay. 30 references. (Author abstract modified)

003656 Budd, Robert D. Rancho Los Amigos Hospital, Downey, CA 90242 **On-column gas chromatographic synthesis of 1,3-dialykyl (C=1-10), benzyl, and cyclohexyl barbiturate derivatives.** Clinical Toxicology. 16(2):189-199, 1980.

Procedures are described for on column gas chromatographic synthesis of various N-alkyl-N-alkyl barbiturates with benzyl or cyclohexyl groups or straight chains with 1 to 10 carbons added to the nitrogens. The 1,3-dialkyl barbiturates with methyl, ethyl, n-propyl, n-butyl, cyclohexyl, isopropyl, or t-butyl groups can be prepared on column by injecting an aliquot of a chloroform solution of the barbiturate with the appropriate N,N-dimethylformamide dialkyl acetal. The 1,3-dialkyl barbiturates with added benzyl or butyl through decyl groups can be similarly prepared with N,N-dimethylformamide dineopentyl acetal and the appropriate alcohol to yield the desired compound. 7 references. (Author abstract modified)

003657 Budd, Robert D. Rancho Los Amigos Hospital, Downey, CA 90242 **Methaqualone RIA structure versus reactivity.** Clinical Toxicology. 16(2):209-217, 1980.

Fourteen methaqualone related substances (substituted 2-methyl-3-phenyl-4-quinazolinones) were analyzed by radioimmunoassay (RIA) at several different concentrations. Structural differences were studied in relation to the affinity of the compounds for Roche RIA methaqualone antibody. The effects of substituent placement on the 2-methyl-3-phenyl-4-quinazolinone molecule were examined. Results showed that addition of a group to the paraposition of the 3-phenyl group increased affinity, whereas alteration of other key functional groups had the reverse effect. 8 references. (Author abstract modified)

003658 Budd, Robert D. Chief Medical Examiner-Coroner, Los Angeles, CA 90033 **Gas chromatographic properties of 1,3-dialkyl barbiturate derivatives.** Clinical Toxicology. 17(3):375-382, 1980.

The gas chromatographic properties of 1,3-dialkyl barbiturates were studied. Retention times (RTs) for 56 1,3-dialkyl derivatives of both aprobarbital and phenobarbital and for 65 1,3-dialkyl derivatives of secobarbital were determined by gas/liquid chromatography. RTs increased with the number of carbons added. A plot of the log of the RT versus the number of carbons in the alkyl group added for 3-alkyl derivatives of 1-alkylbarbiturates was made for the three barbiturates tested. A linear relationship was found for derivatives with butyl or larger groups attached to the second nitrogen of the 1-alkylbarbiturates. The slopes of graphs for 3-alkyl derivatives of 10 1-alkylbarbiturates for each barbiturate studied were identical with a similar plot for straight chain hydrocarbons. This linear relationship permitted calculation of the RTs of large N,N-dialkyl barbiturates, such as N,N-eicosanylsecobarbital, which are not readily synthesized or chromatographed. 2 references. (Author abstract modified)

003659 Budd, Robert D.; Leung, Wai J.; Yang, Felisa C. Chief Medical Examiner-Coroner, Los Angeles, CA 90033 **RIA opiates: structure versus reactivity.** Clinical Toxicology. 17(3):383-393, 1980.

A radioimmunoassay (RIA) was used to analyze 26 opiates at five different concentrations. Structural differences were studied in relation to the affinity of the compounds for the Roche RIA morphine antibody, and the effects of substituent placement on the morphine molecule were examined. Results show that the basic 5-ring opiate structure is essential for activity. Addition of an alkyl group to the oxygen in the 3-position increases affinity, but alteration of other key functional groups has the reverse effect. 10 references. (Author abstract modified)

003660 Clement-Cormier, Yvonne C. Dept. of Pharmacology and Neurobiology, University of Texas Medical School at Houston, Houston, TX 77025 **The dopamine receptor: isolation, purification and regulation.** Research Report, NIMH Grant R03-MH-32431, 1979. 22 p.

A binding protein was extracted with potassium chloride from the microsomal fraction (P3) of the calf striatum. The extract bound (3H) spiroperidol with high affinity and exhibited stereoselectivity for the () and (-) isomers of butaclamol. Results of stability tests indicate that the solubilized component is stable to storage at -20 degrees C for several weeks and at -4 degrees C for 1 week. The IC50 values for displacement of (3H) spiroperidol binding by dopamine and other neuroleptic agents were determined to be similar to those of the native membrane binding component. When the soluble microsomal fraction was extracted with chloroform methanol, stereoselective binding was recovered in both the aqueous and organic solvent phases. Gel filtration chromatography of the soluble membrane preparation revealed three major zones of stereoselective binding activity for (3H) spiroperidol. Protein kinase, which eluted with the molecular weight marker, aldolase, was detected in the KCl-P3 salt extract. The phosphorylation of endogenous proteins with molecular weights corresponding to the molecular weights of the aforementioned peaks was observed. Dopamine in micromolar concentrations increased the phosphorylation of a specific macromolecule eluted from the column. The data support the heterogeneity of the dopamine receptor and suggest that protein phosphorylation may play a role in dopamine receptor binding activity. 16 references. (Author abstract modified)

003661 Clement-Cormier, Yvonne C. University of Texas Medical School at Houston, Dept. of Neurobiology and Pharmacology, P.O.Box 20708, Houston, TX 77025 **Dopamine receptor purification and characterization. (Unpublished paper).** Final Report, NIMH Grant R03-MH-32431, 1979. 9 p.

Characteristics of the dopamine receptor and receptor cyclase complex were analyzed biochemically and pharmacologically. The findings from binding studies of selected ligands to the dopamine receptor revealed a profile for multiple binding sites and the existence of a subpopulation of dopamine recognition sites in the caudatenucleus. They also clarified the discrepancy between the effective potency of haloperidol as an antagonist of dopamine sensitive adenylate-cyclase and its action on binding. The specific binding of (3H) ADTN, a rigid analog of dopamine, to synaptic membranes and micromes also was tested. In receptor topography studies, protoberberine related alkaloids were used to characterize the geometric and sterospecific requirements of antagonists of the dopamine receptor. Optical isomers of selected compounds were tested for their ability to antagonize dopamine stimulated adenylate-cyclase. Receptor solubilization and purification studies demonstrated a close association of the dopamine receptor with phospholipids. Observations of opposite effects on receptor interaction with L-DOPA provided additional support for a multiple class of dopamine receptors. 10 references.

003662 Dettmar, P. W.; Fortune, D.; Lynn, A. G.; Metcalf, G.; Morgan, B. A. Dept. of Pharmacology, Pharmaceutical Division, Reckitt and Colman, Dansom Lane, Kingston-upon-Hull, HU8 7Ds, England **Biological evaluation of a TRH analogue with a modified proline residue.** Neuropharmacology. 19(12):1247-1248, 1980.

An analogue of thyrotropin releasing hormone (TRH), RX 77368 was evaluated in tests designed to probe both the endocrinological and neuropharmacological properties of the molecule, and the results were compared to those obtained with TRH itself, amitryptyline, amphetamine, and doxapram. RX 77368 was found to exhibit prolonged biological stability and enhanced CNS potency compared to the parent peptide. Its profile of neuropharmacological activity overlaps but is not identical with the profiles of tricyclic antidepressant drugs, CNS stimulants, or analeptics. It is contended that such a profile is novel and worthy of clinical evaluation. 5 references.

003663 Faull, Kym F.; Anderson, Patricia J.; DoAmaral, Jefferson R.; Conradson, Steven; Barchas, Jack D.; Berger, Philip A. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **A selected ion monitoring assay for biogenic amine metabolites and probenecid, in human lumbar cerebrospinal fluid.** Journal of Chromatography. 163:337-349, 1979.

Details are presented of a selected ion monitoring assay using combined gas chromatography mass spectrometry for the major biogenic amine metabolites and probenecid in human lumbar CSF. The metabolites and probenecid were simultaneously extracted with ethyl acetate from an acidified aqueous phase and were simultaneously converted to pentafluoropropionyl esters by reaction with pentafluoroproprionic anhydride. The esters of the metabolites were analyzed following a single injection of the derivatized sample onto the gas chromatograph column, while the ester of probenecid was analyzed following a separate injection onto the chromatograph column. Deuterated analogues of the metabolites and a chemical analogue of probenecid were used as internal standards in order to achieve quantitation. Data are presented on the concentration of the metabolites in lumbar CSF taken from healthy volunteers. 10 references. (Author abstract modified)

003664 Fong, Jim C.; Shenkman, Louis; Goldstein, Menek. Goldstein: Neurochemistry Laboratories, Dept. of Medicine, New York University Medical Center, New York, NY 10016 **Purification and characterization of rat pheochromocytoma dopamine beta-hydroxylase.** Journal of Neurochemistry. 34(2):346-350, 1980.

Dopamine beta-hydroxylase (DbetaH) was purified from rat adrenal pheochromocytoma tumors by a procedure that requires only a few purification steps. Tumors obtained from a small number of rats yielded sufficient quantities of pure DbetaH to raise antibodies to DbetaH in guinea-pigs. The specificity of the antiserum was demonstrated by immunoelectrophoretic and Ouchterlony immunodiffusion analysis, as well as by the specific inhibition of DbetaH activity. Enzyme inhibition studies revealed complete cross-reactivity between the rat pheochromocytoma antiserum and rat adrenal DbetaH, but interspecies cross-reactivity was almost nonexistent. The molecular parameters and the kinetic properties of rat pheochromocytoma DbetaH are similar to those reported for bovine adrenal, human plasma, and human pheochromocytoma DbetaH. 22 references. (Author abstract)

003665 Greenfield, S.; Brostoff, S. W.; Hogan, E. L. Dept. of Neurology, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29403 **Characterization of the basic proteins from rodent peripheral nervous system myelin.** Journal of Neurochemistry. 34(2):453-455, 1980.

Electrophoretic evidence that the major staining basic proteins in rat and mouse peripheral nervous system (PNS) myelin correspond in molecular weight to the CNS small and large basic proteins is presented. This clear demonstration of the separate identity and quantitative excess of the PNS analogue of the small CNS myelin basic protein over P2-protein in both rat and mouse PNS myelin was supported by immunological studies. The bands of PNS myelin proteins on SDS gels that corresponded to the large and small CNS basic proteins exhibited cross-reactivity in a radioimmunoassay for myelin basic protein but not in a radioimmunoassay for P2-protein. This supports the conclusion that these two proteins in rat and mouse PNS myelin are analogous to the small and large basic protein of CNS. That the minor band in mouse and rat myelin comigrate with P2-protein also suggests that P2-protein is present in rodent PNS myelin. 9 references.

003666 Huang, H. T.; Lin, H. S.; Lu, K. S. Dept. of Anatomy, College of Medicine, National University, Taipei, Taiwan **Ultrastructural localization of monoamines in nerve fibers of the**

pineal gland in golden hamsters. Journal of Neural Transmission. 45:253-264, 1979.

Nerve terminals in the pineal glands of hamsters treated with nothing, parachlorophenylalanine (PCPA), reserpine, or nialamide were studied with glutaraldehyde dichromate (GD) and formaldehyde glutaraldehyde dichromate (FGD) techniques on the electron microscope. In controls, clusters of electron dense reactive particles mainly located in the perivascular space were identified as dense cores of the small granulated vesicles (SGVs) in the pineal nerve fibers. Reactive cores were: 1) greatly decreased in number after PCPA administration under the FGD technique but not under the GD technique, 2) increased in number and in electron density after administration of nialamide under either technique, and 3) not revealed after reserpine administration under either technique. It is concluded that the dense cores of SGVs in the pineal nerve fibers contain both primary catecholamines and 5-hydroxytryptamine, although it was not determined whether both amines are located in the same or separate vesicles. (Journal abstract modified)

003667 Jatlow, Peter I.; Miller, Ronald; Swigar, Mary. Dept. of Laboratory Medicine and Psychiatry, Yale University School of Medicine, 333 Cedar St., New Haven, CT **Measurement of haloperidol in human plasma using reversed-phase high performance liquid chromatography. (Unpublished paper).** Research Report, NIMH Grant 5P50-MH-30929, 1980. 14 p.

A procedure is described for the measurement of haloperidol in plasma using reversed phase high pressure liquid chromatography and low wavelength (195 nm) ultraviolet detection. Chromatography was performed following a solvent extraction and a micro back extraction into dilute acid. No evaporation step was required. The lower limit of sensitivity was approximately 2 ng/ml. The within day and between day coefficients of variation at a concentration of 5 ng/ml were 5% and 7.3%, respectively. The method may be used in determining dosage and plasma concentrations of this potent antipsychotic drug. 15 references. (Author abstract modified)

003668 Keller, Angelica; Scarna, Helene; Mermet, Anne; Pujol, Jean-Francois. Institut d'Embryologie du CNRS, 49 bis Avenue de la Belle Gabrielle, F-94130 Nogent-sur-Marne, France **Biochemical and immunological properties of the mouse brain enolases purified by a simple method.** Journal of Neurochemistry. 36(4):1389-1397, 1981.

A simple and rapid purification method is presented for the two mouse cerebral isozymes of enolase, E1 and E3. The purity of the preparations was ascertained by electrophoresis under two different conditions. The biochemical and immunological properties of E1 and E3 are compared. Both E1 and E3 are homodimers with a subunit of molecular weight of 50,000. The procedure also yields a semipurfiied fraction of E2. In immunohistological studies, antiE1 and antiE3 sera stain two nonoverlapping populations of cells, astrocytes and neurons, respectively. Results support the view that E1 is similar if not identical to liver enolase. 24 references. (Author abstract modified)

003669 Landgraf, W.; Ermisch, A.; Hess, J. Dept. of Biosciences, University of Leipzig, Leipzig, German Democratic Republic **Indications for a brain uptake of labelled vasopressin and ocytocin and the problem of the blood-brain barrier.** Endokrinologie. 73:77-81, 1979.

Fifteen seconds after intracarotid injection of (125J)-lysine vasopressin, (3H)-ocytocin, tritiated water, or (3H)-inulin, the distribution of radioactivity in 18 regions of the rat brain and in the anterior pituitary was determined. Comparing the concentration of the different tracers (in the percentage of injected radioactivity per gram of brain tissue), it is assumed that a small amount of the labeled neurohormones is taken up by the brain, indicating a penetration of the blood-brain barrier and/or an accumulation within the structures of the barrier system. (Journal abstract)

003670 Merlie, John Paul. A234 Langley Hall, Dept. of Life Sciences, University of Pittsburgh, Pittsburgh, PA 15260 **Immuno detection of ACh receptor in the CNS. (Unpublished paper).** Final Report, NIMH Grant R03-MH-31932, 1979. 7 p.

A radioimmune inhibition assay employing antisera (tested for their ability to detect brain proteins which share antigenic determinants) was used to study the alpha-bungarotoxin binding component in the bovine brain. This neurotoxin has been used as a specific label for ACh receptors in rat skeletal muscle, but there were discrepancies concerning the specificity of its binding to other nicotinic ACh receptors in nervous tissue. The specific aim was to use alpha-bungarotoxin binding and immunological cross-reactivity to identify and characterize ACh receptors from the central nervous system. The initial experiments provided no evidence of alpha-bungarotoxin binding. It is concluded that bovin brain, unlike rat brain, does not contain an alpha-bungarotoxin binding component. The absence of an immunologically related molecule is questionable and further research is necessary.

003671 Muller, H.; Harzer, K. Harzer: Institut fur Hirnforschung, Universitat Tubingen, D-7400 Tubingen, Belthlestrasse 15, West Germany **Partial purification of acid sphingomyelinase from normal and pathological (M. Niemann-Pick type C) human brain.** Journal of Neurochemistry. 34(2):446-448, 1980.

The partial purification of acid sphingomyelinase from normal and pathological human brain (Niemann-Pick disease) using a variation of the procedure of Yamaguchi and Suzuki (1977) is described. Clinically and biochemically, Niemann-Pick disease type-C is an insufficiently defined neurovisceral lipidosis with increased sphingomyelin and other lipid content, predominantly in the spleen, but without clear defect of sphingomyelinase. The present findings of similar properties of sphingomyelinase purified from control and Niemann-Pick disease type-C tissue may provide further evidence against a specific involvement of acid sphingomyelinase in Niemann-Pick disease type-C. The metabolic cause of the disease remains unknown. 10 references.

003672 Nakayama, Takashi. Dept. of Biochemistry, Institute of Brain Research, Tokyo University Faculty of Medicine, Hongo 7-3-1, Bunkyoku, Tokyo, Japan **Synthesis of cytoskeletal proteins in bulk-isolated neuronal perikarya.** Journal of Neurochemistry. 36(4):1398-1405, 1981.

The synthesis of cytoskeletal proteins in bulk isolated rat neuronal perikarya is described. Neuronal perikarya were isolated from young rat brain by sucrose density gradient centrifugation of the tissue, dissociated with a low concentration of trypsin. Neuronal perikarya synthesized predominantly actin, and alpha1-tubulin, alpha2-tubulin, and beta-tubulin. In addition, polypeptides with molecular weights of 35,000, 68,000, and 85,000 were labelled heavily. On two dimensional electrophoresis, microheterogeneities were seen in soluble actin as well as in soluble tubulins, indicating that heterogeneities reported for brain actin and tubulins are inherent in neuronal actin and tubulins, but are not due to the heterogeneity of cells in the brain tissue. 25 references. (Author abstract modified)

003673 Ortiz, A.; Pardo, A.; Fernandez-Alonso, J. I. Depto. de Quimica Fisica y Quimica Cuantica, Centro Coordinado CSIC-UAM, Facultad de Ciencias C-XIV, Cantoblanco, Madrid 34, Spain **Spectra of radical cations of phenothiazine derivatives in**

solution and solid state. Journal of Pharmaceutical Sciences. 69(4):378-380, 1980.

The ultraviolet and visible spectra of radical cations of several phenothiazine derivatives were studied using different solvents. The establishment of a relationship between these bands and the R2 and R10 substituents was attempted. The influence of the disolvents on the bands also was studied. The characteristic charge transfer band was observed in the solid state using diffuse reflectance spectroscopy. The R2 substituent did not appear to influence the band, while the R10 substituent influenced the band considerably, probably due to steric effects. 15 references. (Author abstract)

003674 Ponzio, F.; Achilli, G.; Algeri, S. Algeri: Istituto di Ricerche Farmacologiche Via Eritrea, 62, I-20157 Milan, Italy **A rapid and simple method for the determination of picogram levels of 3-methoxytyramine in brain tissue using liquid chromatography with electrochemical detection.** Journal of Neurochemistry. 36(4):1361-1367, 1981.

A rapid and simple technique using solvent extraction, ion pairing extraction, and high pressure liquid chromatography with electrochemical detection is described for the determination of 3-methoxytyramine in striata of rats killed by microwave irradiation. The method is specific and reproducible; recovery of authentic 3-methoxytyramine added to the samples is 45% to 50%. 3-methoxytyramine levels found with this technique in rat striata were 15ng/g plus or minus 1.7nglg. The method has a sensitivity of about 0.2pmol per brain sample. Monoamine oxidase inhibition with pargyline increased 3-methoxytyramine levels in rat striata, while catechol-0-methyltransferase inhibition with 3′,4′-dihydroxy-2-methylpropiophenone completely depleted 3-methoxytyramine. The effects of nomifensine, quipazine, caroxazone, piribedil, and D-amphetamine were examined. The 3-methoxytyramine concentrations in the brains of animals killed by decapitation or by microwave irradiation were compared. 31 references. (Author abstract modified)

003675 Rumigny, J. F.; Maitre, M.; Cash, C.; Mandel, P. Maitre: Centre de Neurochimie du CNRS, 5, rue Blaise Pascal, F-67000 Strasbourg, France **Regional and subcellular localization in rat brain of the enzymes that can synthesize gamma-hydroxybutyric acid.** Journal of Neurochemistry. 36(4):1433-1438, 1981.

The regional and subcellular localization in rat brain of the two major NADPH linked aldehyde reductases that can reduce succinate semialdehyde to 4-hydroxybutyrate is described. One of the enzymes appears to be fairly specific for succinate semialdehyde and is not inhibited significantly by classical aldehyde reductase inhibitors such as barbituates. The other enzyme can reduce several aromatic aldehydes and is inhibited strongly by barbiturates and branched chain fatty acids. Using one such inhibitor, the activities of the two enzymes were measured separately in various rat brain regions and subcellular fractions. Both enzymes are mainly cytoplasmic but there is some activity in the synaptosomal fraction. The activity of the specific succinic semialdehyde reductase is highest in the cerebellum, where it represents 21% of the total activity, and lowest in the cortex, where it represents about 11% of the total activity. 40 references. (Author abstract modified)

003676 Ryan, Rick; McClure, William O. McClure: Division of Cellular Biology, Dept. of Biological Sciences, University of Southern California, Los Angeles, CA 90007 **Physical and kinetic properties of choline acetyl transferase from rat and bovine brain.** Journal of Neurochemistry. 34(2):395-403, 1980.

Several physical and kinetic properties of highly purified choline acetyltransferase (acetyl-CoA) from rat and bovine brain were investigated. The molecular weight of the enzyme from rat cerebrum was 65,000 measured by gel filtration and 66,000 measured by acrylamide gel electrophoresis in the presence of sodium dodecyl sulfate. Two species of the enzyme detected in bovine caudate nuclei were studied using the same procedures. The major transferase species, bovine-I, yielded values of molecular weights of 69,000 and 70,000, respectively. The minor bovine acetylase species (bovine-II) had a molecular weight of 67,000 daltons by gel filtration. The dependence of reaction rates catalyzed by bovine-I and rat choline acetyltransferase on temperature and pH was examined. 36 references. (Author abstract modified)

003677 Schmidt, Rupert; Shashoua, Victor E. Shashoua: Mailman Research Center, McLean Hospital, Belmont, MA 02178 **A radioimmunoassay for ependymins beta and gamma: two goldfish brain proteins involved in behavioral plasticity.** Journal of Neurochemistry. 36(4):1368-1377, 1981.

A radioimmunoassay (RIA) using 125I-labeled antigen was developed for the quantitative determination of two goldfish brain proteins (ependymins beta and gamma). The proteins were isolated from cerebrospinal fluid (CSF) and cells of the ependymal zone surrounding goldfish brain ventricles. The turnover rates of beta and gamma were shown previously to be enhanced specifically after the animals successfully acquired a new pattern of swimming behavior. Femtomole quantities of ependymin beta were measurable by the RIA. In applications of the assay, beta and gamma ependymins were found to have common immunological properties, since 125I-beta-antigen bound to antibody could be displaced by unlabeled ependymin gamma as well as by ependymin beta, but not by a variety of other proteins including several purified glycoproteins isolated from goldfish brain. The data suggest that the antigenitic of the molecules is masked highly, and that it may require some unraveling of the quaternary structure of the proteins before maximal interaction with the antisera becomes possible. 20 references. (Author abstract modified)

003678 Viles, Joseph M. Iowa State University, Ames, IA 50010 **Satiety center neuroanatomy. (Unpublished paper).** Final Report, NIMH Grant R03-MH-32916, 1980. 7 p.

The specific glucoreceptor cells of the mouse ventromedial hypothalamus were identified and were morphologically characterized using microscopic analysis of the area following pharmacological modification of the satiety center with gold thioglucose (GTG) administration. The findings from transmission electron micrographs of tissue taken at very early stages (1 hour) following macrolesion GTG treatment, as well as later stages (4 to 6 hours) following microlesion GTG treatment indicated that the primary lesion is perivascular, involving what appears to be oligodendroglia. The data showed that there is no direct participation of putative glucoreceptor neurons in the primary lesioning process. The pathology of the microlesion, which results in impairment of the control of feeding behavior and which presumably reflects specific neuronal damage, develops very rapidly, and results in a condition of acellularity in the lesioned area by 12 hours following a macrolesion GTG dose. Examination by electron microscopy in the early stages of lesion development following macrolesion GTG doses and during microlesion development revealed ultrastructural evidence of capillary breakdown due to inflammatory processes.

003679 Yamamoto, H.; Takahashi, Yasuo. Takahashi: Dept. of Neuropharmacology, Brain Research Institute, Niigata University, Asahimachi, Niigata 951, Japan **Purification and subunit structure of DNA-dependent RNA polymerase BII from rat brain nuclei.** Journal of Neurochemistry. 34(2):255-260, 1980.

DNA dependent RNA polymerase BII from rat brain nuclei was purified by ammonium sulphate fractionation, successive chromatography on ion exchange resins, and glycerol density gradient centrifugation. The purified enzyme was resolved into two components (BIIa and BIIb) on native polyacrylamide gel electrophoresis. The subunit compositions of these enzymes were analyzed on SDS-polyacrylamide gels. BIIa enzyme consisted of nine subunits (molecular weights of 215,000, 150,000, 35,000, 25,000, 21,500, 17,500, 15,500, 14,500, and 11,500). BIIb enzyme also consisted of nine subunits, with the highest molecular weight subunit at 180,000 and the remaining eight subunits equal to those of BIIa. Addition of both 30% glycerol and dithiothreitol to the preparation medium was essential for stabilizing the enzyme. 18 references. (Author abstract modified)

003680 Yasunobu, Kerry T., Zeidan, Hussein; Ishizaki, Hiroyuki. Dept. of Biochemistry-Biophysics, University of Hawaii, Honolulu, HI 96822 **Cu-amine oxidases: studies related to the mechanism of action of bovine plasma amine oxidase. (Unpublished paper).** Research Report, NIMH Grant MH-21539, 1979. 24 p.

The status of knowledge on the mechanism of action of bovine plasma amine oxidase is discussed, and new findings are presented. The use of nitroxide spin labeled N-ethylmaleimide reagents confirmed the liberation of two sulfhydryl groups by substrate. Probing the domain in which these sulfhydryl groups are present indicated that they occur in a very shallow pocket in the subsite of the active center of the enzyme. In the substrate reduced form of the enzyme trapped by anaerobiesis, the copper is over 14,angstroms apart from the sulfhydryl group which is liberated by substrate. The reaction of the enzyme with hydrazine derivatives was extended and it was found to liberate the same sulfhydryl groups that are liberated by substrate. Therefore, the initial enzyme substrate complex appears to involve the formation of a complex in which N of the hydrazine derivative and the organic cofactor form a bond. The CD spectra of the enzyme-hydrazine derivatives disclosed that the complexes are active optically, which indicates that an asymmetrical complex exists. The ESR spectra of these derivatives suggested that copper is not involved directly in complex formation. Research in progress concerning the structure of the cofactor and the binding of copper to the enzyme is discussed. 20 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

003681 Al'tshuler, R. A.; Mashkovskiy, M. D. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonikidze, Moskva, USSR **/The pharmacological action of the optical isomers of sydnocarb./** Farmakologicheskaya aktivnost' opticheskikh izomerov sidnokarba. Farmakologiya i Toksikologiya. 43(4):345-349, 1980.

The pharmacological action of the optical isomers of sydnocarb was studied in mice and rats. Results show that of the two optical isomers of sydnocarb only the 1-(1R)-isomer stimulates the CNS; by its stimulant action it differs from both optical isomers of amphetamine. Results also show that the activity of 1-(1R)-sydnocarb, as measured by the locomotor excitation test, is similar to that of d(1S)-amphetamine, but is significantly less powerful, as indicated by stereotypy, hypothermia, anorexigenic action, and antagonism to the depressant effects of reserpine. 9 references. (Journal abstract modified)

003682 Audigier, Yves; Mazarguil, Honore; Gout, Robert; Cros, Jean. Laboratoire de Pharmacologie et de Toxicologie Fondamentales. CNRS, 205, route de Narbonne, F-31078 Toulouse Cedex, France **Synthesis and pharmacological study of some enkephalin analogs in relation to the plurality of opiate receptors.** European Journal of Medicinal Chemistry. 15(2):173-177, 1980.

A series of enkephalin analogs was synthesized, and their affinity for the mu and delta opioid receptors was evaluated. Their individual antinociceptive activities when intracerebroventricularly injected were studied. Chemical structure was found to correlate with selective binding to each type of receptor. Analgesic activity induced by the (Met)5 analogs and the (Leu)5 analogs was found to be correlated with affinity for the mu-receptor. Analgesic activity of (Pro)5 analogs was also correlated with mu-receptor. Analgesic activity of (Pro)5 analogs was also correlated with mu-receptor affinity, but was much greater than could be predicted by mu-affinity alone. 14 references. (Author abstract modified)

003683 Braun, Ulrich; Shulgin, Alexander T.; Braun, Gisela. Shulgin: 1483 Shulgin Road, Lafayette, CA 94549 **Centrally active N-substituted analogs of 3,4-methylenedioxyphenylisopropylamine (3,4-methylenedioxyamphetamine).** Journal of Pharmaceutical Sciences. 69(2):192-195, 1980.

The CNS activity of 3,4-methylenedioxyphenylisopropylamine and its N-methyl homolog prompted the synthesis of a series of analogs with substituents on the nitrogen atom. Most of these analogs were prepared by reductive alkylation of 3,4-methylenedioxyphenylacetone with the appropriate amine and sodium cyanoborohydride. Hindered isomers were synthesized indirectly. Measurements of pharmacological activity in several animal assays and in human Ss indicated that central activity decreased with the increasing bulk of the N-substituent. 23 references. (Author abstract modified)

003684 Chipkin, Richard E.; Morris, Dan H.; English, Michael G.; Rosamond, James D.; Stammer, Charles H.; York, Eunice J.; Stewart, John M. Dept. of Biochemistry, University of Colorado School of Medicine, Denver, CO 80262 **Potent tetrapeptide enkephalins.** Life Sciences. 28(13):1517-1522, 1981.

The synthesis and biological activities of enkephalin tetrapeptides in which glycine has been deleted are described. It is noted that small peptides with opiate-like activity have generally had structures closely resembling that of the opioid pentapeptide enkephalin: Tyr-Gly-Gly-Phe-Met-COOH. Single deletions of any one of the amino acids has been demonstrated to reduce opiate activity drastically. Potency losses resulting from the removal of glycine were fully attenuated by substitution of D-alanine in position two and derivatization of the acid to the amide. This tetrapeptide (Tyr-DAla-Phe-Met-NH2) has narcotic activity similar to the parent pentapeptide in the guinea-pig ileum and mouse tail flick tests. This enhanced potency, relative to the unaltered tetrapeptide, is theorized to arise from increased resistance to enzymatic destruction. The data presented show that a five amino acid sequence is not mandatory for the expression of opiate activity in enkephalin analogs. 19 references. (Author abstract modified)

003685 Correa, F. M. A.; Innis, R. B.; Rouot, B.; Pasternak, G. W.; Snyder, S. H. Dept. of Pharmacology and Experimental Ther., Johns Hopkins University School of Medicine, Baltimore, MD 21305 **Fluorescent probes of alpha- and beta-adrenergic and opiate receptors: biochemical and histochemical evaluation.** Neuroscience Letters. 16:47-53, 1980.

Dansyl derivatives of the opiate antagonist naloxazone and the alpha-adrenergic blocking drug 2-((2',6'-dimethoxy)phenoxyethylamino)methylbenzodioxan (WB-4101) were synthesized as potential in vivo fluorescent labels for opiate and alpha-adrenergic receptors, respectively. When assayed in vitro, dansyl analogs displayed Ki values for

(3H)naloxone and (3H)WB-4101 binding of 8nM and 80nM, respectively. The same patterns of histofluorescence were observed in rat brain slices after the intravenous or intracerebroventricular injection of both dansyl drugs. The same patterns were seen in dansyl-propranolol and 9-aminoacridine-propranolol treated animals, as well as in untreated control rats. It is concluded that the observed fluorescence does not reflect the labeling of any receptor, but is consistent with the distribution of lipofuscin and an endogenous fluorescent compound. (Journal abstract modified)

003686 Diggory, G. L.; Stephens, R. J.; Dickison, S. E.; Moser, P.; Wood, M. D. Biochemical Pharmacology Laboratory, Wyeth Institute of Medical Research, Huntercombe Lane South, Taplow, Maidenhead, England **Behavioural and neurochemical properties of 1-(1-((indol-3-yl) methyl) piperid-4-yl)-3-benzoylurea (Wy 25093) in rodents.** Archives Internationales de Pharmacodynamie et de Therapie. 248(1):86-104, 1980.

Studies in mice and rats showed that 1-(1-((indol-3-yl) methyl) piperid-4-yl)-3-benzoylurea (Wy-25093), a potential antidepressant, was a selective and potent inhibitor of neuronal reuptake of 5-hydroxytryptamine (5-HT). The compound was more potent than clomipramine and fluoxetine as a 5-HT uptake inhibitor in vitro and did not significantly inhibit catecholamine uptake. Wy-25093 potentiated the behavioral syndrome induced by 5-hydroxytryptophan and antagonized the hyperactivity induced by p-chloroamphetamine (P-CA). It antagonized the P-CA induced depletion of 5-HT in rat brain and reduced the probenecid induced increase in 5-hydroxyindole-3-acetic acid (5-HIAA). Acute administration of Wy-25093 reduced 5-HIAA levels without affecting 5-HT, whereas chronic treatment reduced both 5-HIAA and 5-HT. 40 references. (Author abstract modified)

003687 Ellis, K. O.; Schwan, T. J.; Wessels, F. L.; Miles, N. J. Division of Biological Research, Scientific Affairs Dept., Norwich-Eaton Pharmaceuticals, Norwich, NY 13815 **1-(Substituted benzyl)-3,4,5,6-tetrahydro-2(1H)-pyrimidones: a series with stimulant and depressant activities.** Journal of Pharmaceutical Sciences. 69(10):1194-1198, 1980.

A series of 1-(substituted benzyl)-3,4,5,6-tetrahydro-2(1H)-pyrimidones was synthesized, primarily by catalytic hydrogenation of the corresponding 1-(substituted benzyl)-2(1H)-pyrimidone, and the CNS stimulant and depressant properties of the series were assessed. Pharmacological evaluation of these compounds in mice revealed a unique profile that inlcudes evidence of CNS stimulation and depression within the series and in the same compounds. Some members of this series induced signs of only CNS stimulation, some compounds caused signs of only CNS depression and skeletal muscle relaxation, and some caused signs of both stimulation and depression in the same animal. This apparent dual activity was assessed further in mice with antidepressant tests based on tetrabenazine antagonism and with antianxiety/anticonvulsant tests on the antagonism of a number of convulsants. The 4-chloro, 4-fluoro, 4-bromo, and 3,4-dichlorobenzyl compounds exhibited antidepressant and antianxiety activities in the same dose range. 11 references. (Author abstract modified)

003688 Ellis, K. O.; Wessels, F. L.; Burns, R. H.; Pong, S. F. Division of Biological Research, Scientific Affairs Dept., Norwich-Eaton Pharmaceuticals, Norwich, NY 13815 **Pharmacology of 1-(3,4-dichlorobenzyl)-3,4,5,6-tetrahydro-2(1H) pyrimidone, a novel antidepressant compound with antianxiety activity.** Journal of Pharmaceutical Sciences. 69(10):1198-1202, 1980.

1-(3,4-Dichlorobenzyl)-3,4,5,6-tetrahydro-2(1H)-pyrimidone was evaluated in selected pharmacological tests, and its activity was compared to that of some clinically useful psychotropic drugs. Based on the results, it is evident that 1-(3,4-dichlorobenzyl)-3,4,5,6-tetrahydro-2(1H)-pyrimidone has a unique profile of antidepressant and antianxiety activities that are evident in the same dose range. The mechanism of its antidepressant activity is proposed to be similar to the tricyclic antidepressants, that is, inhibition of norepinephrine uptake. Neither the experimental compound nor the tricyclic antidepressants possess monoamine oxidase inhibiting activity. Hoever, unlike the tricyclic antidepressants, the experimental compound is devoid of any significant anticholinergic activity and presumably is free of anticholinergic side-effects. 22 references. (Author abstract modified)

003689 Foussard-Blanpin, Odette; Uchida-Ernouf, Genevieve; Anatol, Jesus; Berecoechea, Jean. Lab. de Pharmacodynamie, UER des Sciences Pharmaceutiques, 2 bis, boulevard Tonnelle, F-37032 Tours Cedex, France **/Acylcyanamides, acylurea, and various substituted aryl allophanates; effect on the CNS./** Acylcyanamides, acyluree, aryl allophanates d'ethyle diversement substitues; action sur le systeme nerveux central. European Journal of Medicinal Chemistry. 14(3):215-218, 1979.

A series of substituted ethyl aryl allophanates was synthesized and tested for biological activity in male Swiss mice. The compounds were central nervous system depressants, and some had sedative, analgesic, or anticonvulsant properties. The o-substituted ethyl-2 aryl allophanates appeared to be the most active. 9 references. (Author abstract modified)

003690 Glennon, Richard A.; Doot, Dianne Leming; Young, Richard. Dept. of Pharmaceutical Chemistry, School of Pharmacy, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **DOM and related 2,5-dimethoxy-4-alkylphenylisopropylamines: behavioral and serotonin receptor properties.** Pharmacology Biochemistry and Behavior. 14(3):287-292, 1981.

The 4-methyl (DOM), ethyl (DOET), propyl (DOPR), butyl (DOBU), tertiary butyl (DOTB), and amyl (DOAM) derivatives of 2,5-dimethoxy-phenylisopropylamine had similar serotonin receptor affinities in the male Sprague-Dawley rat isolated fundus preparation. All of the compounds interacted in an agonistic manner with serotonin and phenoxybenzamine resistant tryptamine receptors. Administration of DOET, DOPR, DOBU, DOTB, and DOAM to rats trained to discriminate 5-methoxy-N,N-dimethyltryptamine from saline produced only partial generalization. 31 references. (Author abstract modified)

003691 Grouiller, Annie; Nioche, Jean-Yves; Barailler, Josiane; Roche, Maurice; Pacheco, Henri. Laboratoire de Chimie Biologique, I.N.S.A., Bat. 406, 20, avenue Albert Einstein, F-69621 Villeurbanne Cedex, France **/Synthesis and biochemical and pharmacologic properties of analogues and derivatives of p.chlorophenylalanine./** Analogues et derives de la p.chlorophenylalanine: synthese, proprietes biochimiques et pharmacologiques. European Journal of Medicinal Chemistry. 15(2):139-146, 1980.

Analogs of p. chlorophenylalanine in indane, tetraline, and phenylcyclopropane series and esters and methylamino derivatives of this amino acid were synthesized. They were assayed in vitro on four enzymes of the rat brain which are implicated in the biosynthesis of serotonin and dopamine. Their activity on the sleep/wakefulness rhythm was studied in the rabbit via electrophysiological methods. 31 references. (Author abstract modified)

003692 Hirose, K.; Matsushita, A.; Eigyo, M.; Jyoyama, H.; Fujita, A.; Tsukinoki, Y.; Shiomi, T.; Matsubara, K. Matsushita: Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553, Japan **Pharmacology of 2-o-chlorobenzoyl-4-chloro-N-methyl-Na glycylglycinanilide hydrate (45-0088-S), a compound with benzodiazepine-like properties.** Arzneimittel-Forschung. 31(1):63-69, 1981.

The pharmacological properties are discussed of 2-o-chlorobenzoyl-4-chloro-N-methyl-Na-glycylglycinanilide hydrate (45-0088-S), a novel dipeptido-aminobenzophenone compound. 45-0088-S, an open ring derivative of 1,4-benzodiazepine, was compared chemically and clinically to chlordiazepoxide, medazepam, diazepam, and imipramine hydrochloride. Data are provided for the following experimental parameters concerning 45-0088-S: acute toxicity in mice; behavioral observation in mice and rats (spontaneous motor activity, open-field test); antimuricide activity in rats; muscle relaxation in mice and cats; hypothermic activity, antifighting activity, and anticonvulsant activity in mice; effect on shuttlebox avoidance in mice and rats; effect on distracted reaction in rats; and effect on conflict behavior in rats and monkeys. 45-0088-S inhibited pentetrazole induced conflict behavior in rats and monkeys, and induced muscle relaxation in cats at lower doses than did diazepam. The pharmacological profile of 45-0088-S suggests that it can be an active, water soluble antianxiety agent in humans. 16 references. (Journal abstract modified)

003693 Honore, Tage; Hjeds, Hans. Royal Danish School of Pharmacy, Dept. of Chemistry BC, DK-2100 Copenhagen 0, Denmark **Synthesis and GABA-receptor binding activity of two fluoroaminomethylphenols.** European Journal of Medicinal Chemistry. 14(3):285-287, 1979.

The fluoroaminomethylphenols 2-fluoro-5-aminomethylphenol and 2,4-difluoro-5-aminomethylphenol were synthesized and evaluated for effects on GABA binding to rat brain membranes. Both compounds were weak inhibitors of 3H-GABA binding. 12 references. (Author abstract modified)

003694 Kalix, Peter. Department de Pharmacologie, Universite de Geneve, Rue Ecole-de-Medecine 20, CH-1211 Geneve 4, Switzerland **Hyperthermic response to (-)-cathinone, an alkaloid of Catha edulis (khat).** Journal of Pharmacy and Pharmacology. 32(9):662-663, 1980.

A new khat alkaloid of the phenylethylamine type, (-)-cathinone, induced hyperthermia in restrained rabbits. The hyperthermic effect of (-)-cathinone was reduced by pretreatment with pimozide and blocked by pretreatment with haloperidol. The effects of (-)-cathinone were similar to those of ()-amphetamine and suggest that the two substances act by the same mechanism. 7 references.

003695 Kornet, Milton J. College of Pharmacy, University of Kentucky, Lexington, KY 40506 **Synthesis of phenylurethans of 1,2-dialkyl-4-pyrazolidinols as anticonvulsant agents.** Journal of Pharmaceutical Sciences. 69(6):729-731, 1980.

Twelve phenylurethans of 1,2-dialkyl-4-pyrazolidinols were synthesized and were tested for anticonvulsant activity. The necessary 1,2-dialkyl-4-pyrazolidinols were obtained from the reaction of epichlorohydrin and 1,2-dialkylhydrazines according to a previously reported procedure. Hydrazinoalcohols possessing methyl, ethyl, and n-propyl substituents were prepared. Compounds were examined in the maximal electroshock seizure and subcutaneous pentylenetetrazol seizure threshold tests for anticonvulsant activity and neurotoxicity in male mice. Several compounds exhibited anticonvulsant activity. 5 references. (Author abstract modified)

003696 Krulik, R.; Farska, I.; Prokes, J.; Tykva, R. Psychiatry Research Unit, Medical School, Charles University, Ke Karlovu 11, Prague 2, Czechoslovakia **Distribution of cesium in the organism and its effect on the nucleotide metabolism enzymes.** International Pharmacopsychiatry. 15(3):157-165, 1980.

Distribution of cesium in various tissues of the rat and mouse and the effect on nucleotide metabolism enzymes were studied following a single dose of cesium chloride. In the mouse, maximum cesium levels were reached in the kidneys, heart, lungs, and liver in the first hour, in the muscles after 8 hours, in the brain after 24 hours, and in the blood after 24 hours. Rats excreted 17% of the dose in 24 hours and 38% in 144 hours. In rats, equalization of plasma and red blood cell cesium levels took longer than 6 hours. Cesium transport was not entirely dependent on the ATPase system, as shown by the results given by the crude mitochondrial fraction with a reduced potassium content. Among the various univalent ions studied, the effect of cesium on creating kinase, 5'-nucleotidase, phosphodiesterase and deaminase activity was the smallest. Cesium's relatively low toxicity and low level of metabolic changes strongly suggest that clinical tests with psychiatric patients might be successful. 20 references. (Author abstract modified)

003697 O'Donnell, John P.; Azzaro, A. J.; Urquilla, P. R. School of Pharmacy, West Virginia University Medical Center, Morgantown, WV 26506 **Preparation and biological actions of N-2,2,2-trifluoroethyl-2-(3,4 dihydroxyphenyl)ethylamine.** Journal of Pharmaceutical Sciences. 69(2):149-152, 1980.

In an attempt to develop new dopaminergic drugs for the treatment of parkinsonism, N-2,2,2-trifluoroethyl-2-(3,4-dihydroxyphenyl)ethylamine was synthesized and compared to N-ethyl-2-(3,4-dihydroxyphenyl)ethylamine and dopamine. Dopamine and the N-ethyldopamine analog both stimulated adenylate cyclase activity in male Sprague-Dawley rat striatum in a dose dependent manner, but the N-trifluoroethyldopamine analog had only a weak effect. The N-ethyldopamine and N-trifluoroethyldopamine analogs both had relaxant effects in isolated rabbit renal and ear arteries, but neither showed selectivity for dopamine receptors. 26 references. (Author abstract modified)

003698 Papadopoulou-Daifotis, Z.; Costakis, Evan; Tsatsas, Georges; Varonos, D. Laboratory of Chemical Pharmacology, University of Athens, Athens, Greece **/Synthesis and pharmacological activity of some 2-imino-3-alkyl thiazoline derivatives./** Synthese et activite pharmacologique de quelques derives de l'imino-2 alkyl-3 thiazoline. European Journal of Medicinal Chemistry. 14(3):253-256, 1979.

New 2-alkylaminoacylimino-3-alkyl-thiazolines were synthesized and tested for pharmacological activity in male mice. Some of the products demonstrated sedative or tranquilizing action and had antiaggressive effects. Some of the compounds exhibited antiinflammatory effects. 12 references. (Author abstract modified)

003699 Popp, F. D.; Parson, R.; Donigan, B. E. Dept. of Chemistry, University of Missouri-Kansas City, Kansas City, MO 64110 **Synthesis of potential anticonvulsants: condensation of isatins with acetone and related ketones.** Journal of Pharmaceutical Sciences. 69(10):1235-1237, 1980.

Substituted isatins were condensed with acetone and other ketones to give analogs of 3-hydroxy-3-acetonyloxindole, and the anticonvulsant activity of the resultant compounds was assessed. Some of these alcohols were dehydrated and several compounds with anticonvulsant activity were obtained. It appears that 3-hydroxy-3-acetonyloxindole is the most potent compound in this series in the maximal electroshock seizure test. 7 references. (Author abstract modified)

003700 Powers, Debra L.; Sowell, J. Walter, Sr., Freeman, J. J.; Kosh, J. W. Division of Pharmacology, College of Pharmacy, University of South Carolina, Columbia, SC 29208 **Anticonvulsant properties of selected pyrrolo(2,3-d)pyrimidine-2,4-diones and intermediates.** Journal of Pharmaceutical Sciences. 69(4):473-476, 1980.

A series of pyrrol(2,3-d)pyrimidine-2,4-diones and intermediates was tested for anticonvulsant activity in mice. Eleven of the 15 compounds possessed anticonvulsant activity against pentylenetetrazol induced convulsions. One compound afforded more anticonvulsant protection against pentylenetetrazol than did trimethadione (67% and 50%, respectively). A suspension of this compound was found to be as effective as a solution in producing anticonvulsant activity. The results suggest that the nitrile analogs were more potent compared to the carbamyl analog due to higher lipid solubility. 14 references. (Author abstract)

003701 Resul, B.; Lewander, T.; Zetterstrom, T.; Ringdahl, B.; Muhi-Eldeen, Z.; Dahlbom, R. Dahlbom: Dept. of Organic Pharmaceutical Chemistry, University of Uppsala, Box 574, S-751 23 Uppsala, Sweden **Synthesis and pharmacological properties of N-(4-(1-azetidinyl)-2-butynyl)-2-pyrrolidone, a highly potent oxotremorine-like agent.** Journal of Pharmacy and Pharmacology. 32(6):439-440, 1980.

An azetidine analogue of oxotremorine, N-(4-(1-azetidinyl)-2-butynyl)-2-pyrrolidone, was synthesized and tested for pharmacological activity in mice and rats. The analogue elicited all symptoms usually observed after oxotremorine administration, including tremor, head twitch, hypokinesia, rigidity, lacrimation, salivation, diarrhea, and hypothermia. Peak responses occurred 30 minutes after administration of oxotremorine or its analogue, but the analogue had a slightly longer duration of action and was nearly twice as potent as oxotremorine. Pretreatment with atropine blocked the effects of oxotremorine and the azetidine analogue. 12 references.

003702 Simon, L. D.; Simon, F. R.; Mohasci, E.; Berger, L.; Simon, E. J. New York University Medical Center, New York, NY 10016 **Effect of the position of the phenolic group in morphinans on their affinity for opiate receptor binding.** Life Sciences. 28(24):2769-2772, 1981.

Homologous series of N-methyl, N-allyl, and N-cyclopropylmethyl-morphinans, differing only in the position of the phenolic hydroxy group, were examined with respect to their binding affinities for the opiate receptor. IC50's were determined for competition with 3H-naltrexone in the presence and absence of 100 mM NaCl. While the compounds with the hydroxy in the 3 position had the highest affinity, the corresponding molecules with the hydroxy in the 2 position or 4 position had significant binding affinity ranging from 30 nM in the cyclopropylmethyl series to 400nM for the 2-hydroxy N-methyl morphinan. The sodium indices were also very similiar to those of the corresponding 3-hydroxy compounds. The only 1-hydroxy derivative available was about fivefold weaker than the corresponding 2-hydroxy and 4-hydroxy compounds. Covering or removing the hydroxy group greatly weakened the binding but did not totally destroy it. There was good correlation between binding affinity and pharmacological potency for all except the methoxy compounds. Their high potency is consonant with in vivo hydrolysis of the methyl ether. 9 references. (Author abstract)

003703 Susic, Veselinka; Masirevic, Gordana. Dept. of Physiology, School of Medicine, University of Belgrade, Visegradska 26/II, 11 000 Belgrade, Yugoslavia **Effects of repeated administrations of dihydroergotoxine (Redergine) on the sleep-wakefulness cycle in the cat.** Gerontology. 27(1,2):1-6, 1981.

The action of chronic administration of dihydroergotoxine (DHET) on the sleep wakefulness cycle of the cat was investigated, with particular attention to the increase in slow-wave sleep (SWS). DHET was administered intraperitoneally at a dose of 1mg/kg for 5 days. Results indicate that DHET acts on the sleep wakefulness cycle by increasing wakefulness and SWS and decreasing rapid eye movement sleep. The effects were fairly stable but had a tendency to diminish with time. Such alterations in the sleep wakefulness are possible indices of the beneficial effects seen in elderly human patients treated with DHET. 34 references. (Author abstract modified)

003704 Ursin, Reidun. Institute of Physiology, University of Bergen, Arstadveien 19, N-5000 Bergen, Norway **Does para-chlorophenylalanine produce disturbed waking, disturbed sleep or activation by ponto-geniculo-occipital waves in cats?** Waking and Sleeping. 4(3):211-221, 1980.

The effect of para-chlorophenylalanine (PCPA) on wakefulness and sleep in the cat was examined with particular emphasis on the waking state and on the ponto-geniculo-occipital (PGO) activity. Sleep waking stages and PGO activity were continuously recorded for 2 days following a control injection and for 5 days following a single injection of 200mg/kg PCPA. Following PCPA, quiet waking with desynchronized EEG activity was increased and waking with synchronous EEG activity was reduced. Active waking was not changed. Sleep was reduced following PCPA, in particular slow-wave sleep with slow synchronous waves. The distribution of PGO activity on the sleep waking stages was altered after administration of PCPA. The sleep waking changes preceded the PGO wave redistribution by 12 to 18 hours. Data do not support the PGO wave activation hypothesis for the sleep loss following PCPA administration. It is concluded that PCPA affects a deactivating, possibly slow-wave producing mechanism, affecting relaxed waking and deep slow-wave sleep but not sleep per se. 11 references. (Author abstract modified)

003705 Valzelli, L.; Bernasconi, S.; Sala, A. Istituto di Ricerche Farmacologiche Via Eritrea 62, I-20157 Milano, Italy **Piracetam activity may differ according to the age of the recipient mouse.** International Pharmacopsychiatry. 15(3):150-156, 1980.

Piracetam was administered to young and old mice in order to investigate whether age modifies the activity of this relatively new, centrally acting drug. After piracetam administration, old mice showed a notably greater increase in brain tryptophan than young animals. Furthermore, piracetam significantly improved the learning capacity of young mice, but was remarkably more active in improving the performance of old mice. These results suggest that piracetam is especially effective in restoring the neurobiological setting of the aging brain. 39 references. (Author abstract)

003706 Watling, K. J. Biological Laboratories, Harvard University, Cambridge, MA 02138 **Stereospecific inhibition of dopamine-sensitive adenylate cyclase in carp retina by the enantioners of (/-)-1-cyclopropylmethyl-4-(3-trifluoromethylthio-5H dibenzo(a,d)cyclohepten-5-ylidene) piperidine (CTC).** Journal of Pharmacy and Pharmacology. 32(11):778-779, 1980.

The effect of 1-cyclopropylmethyl-4-(3-trifluoromethylthio-5H-dibenzo(a,d)cyclohep- ten-5-ylidene) piperidine (CTC) on dopamine stimulated adenylate cyclase activity was studied in carp retina. Results showed that (-)-CTC is a potent antagonist of dopamine sensitive adenylate cyclase, whereas ()-CTC is essentially inactive. These findings suggest that the enantiomers of CTC may be useful tools in the study of dopamine receptors in the CNS. 6 references.

003707 Watzman, Nathan; Buckley, Joseph P. Buckley: College of Pharmacy, University of Houston, Houston, TX 77004 **Comparative analgesic, behavioral, and dependence properties of morphine and 0-(4-methoxylphenylcarbamoyl)-3 diethylaminopropiophenone oxime hydrochloride.** Journal of Pharmaceutical Sciences. 69(2):225-226, 1980.

The analgesic activity of 0-(4-methoxylphenylcarbamoyl)-3-diethylaminopropiophenone oxime hydrochloride was investigated in electroshock tests in male Swiss-Webster mice. The analgesic potency of 0-(4-methoxylphenylcarbamoyl)-3-diethylaminopropiophenone oxime hydrochloride was equal to or greater than that of morphine. Neither nalorphine nor withdrawal produced visible behavioral effects in male Sprague-Dawley rats treated with 0-(4-methoxylphenylcarbamoyl)-3-diethylaminopropiophenone oxime hydrochloride for 21 days, suggesting the physical dependency liability of the compound may be less than that of morphine. 7 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

003708 Ahluwalia, P.; Singhal, R. L. Dept. of Pharmacology, Faculty of Health Sciences, School of Medicine, University of Ottawa, Ottawa, Ontario K1N 9A9, Canada **Effect of low-dose lithium administration and subsequent withdrawal on biogenic amines in rat brain.** British Journal of Pharmacology. 71(2):601-607, 1980.

The effects of low dose lithium administration (2mEq/kg/day) and its subsequent withdrawal on brain biogenic amines were studied in male Sprague-Dawley rats. Levels of striatal tyrosine and midbrain tryptophan were increased after lithium administration, while striatal tyrosine hydroxylase and midbrain tryptophan hydroxylase activities were slightly decreased. Withdrawal resulted in a decrease in tyrosine content and increases in tyrosin hydroxylase activity, tryptophan level, and tryptophan hydroxlase activity. Lithium treatment and withdrawal caused regional changes in levels of noradrenaline and dopamine and decreased levels of 3-methoxy-4-hydroxyphenylglycol and 3,4-dihydroxyphenylacetic acid. Homovanillic acid decreased as a result of lithium treatment, but was greatly elevated after withdrawal. Levels of 5-hydroxytryptamine decreased in some brain regions after lithium treatment, but returned toward control values after withdrawal. Levels of 5-hydroxyindoleacetic acid also showed regional variation as a result of lithium treatment and withdrawal. 35 references. (Author abstract modified)

003709 Ahnert-Hilger, Gudrun; Habermann, Ernst. Rudolf-Buchheim-Institut fur Pharmakologie der Justus-Liebig-Universitat Giessen, Frankfurter Strasse 107, D-6300 Giessen, West Germany **Increase of cGMP and accumulation of 45Ca2 evoked by drugs acting on sodium or potassium channels.** European Journal of Pharmacology. 70(3):301-310, 1981.

Cyclic guanosine monophosphate (cGMP) and labeled calcium ion (45Ca2) accumulation were measured in adult NMRI mouse cerebellar slices after treatment with compounds that affect ion channels in excitable membranes. Cyclic GMP and 45Ca2 were elevated by scorpion toxin and sea anemone toxin-II, which keep the activated sodium channel open, and by 4-aminopyridine and tetraethylammonium, which block potassium conductance. Tetrodotoxin inhibited the effects of these four drugs, but did not inhibit the effect of depolarizing concentrations of potassium. The cyclic GMP content of nonexcitable cells, such as isolated hepatocytes from rat and guinea-pig, was not affected in a comparable manner. It is concluded that in excitable cells, sodium influx triggers an increase in intracellular free calcium and cyclic GMP and that this effect is independent of the ion channel primarily affected. 40 references. (Author abstract modified)

003710 Akasu, Takashi; Hirai, Keiji; Koketsu, Kyozo. Dept. of Physiology, Kurume University School of Medicine, Kurume 830, Japan **5-Hydroxytryptamine controls ACh-receptor sensitivity of bullfrog sympathetic ganglion cells.** Brain Research. 211(1):217-220, 1981.

The direct interaction of 5-hydroxytryptamine (5-HT) with nicotinic acetylcholine (ACh) receptors was demonstrated in bullfrog sympathetic ganglion cells and frog skeletal muscle endplates. The action of 5-HT was comparable to that of d-tubocurarine, suggesting that 5-HT may decrease the affinity of ACh for nicotinic receptor sites. 7 references. (Author abstract modified)

003711 Ali, B. H.; Bartlet, A. L. Dept. of Veterinary Pharmacology, University of Edinburgh, Edinburgh, EH9 1QH, England **Inhibition of monoamine oxidase by furazolidone in the chicken and the influence of the alimentary flora thereon.** British Journal of Pharmacology. 71(1):219-224, 1980.

Monoamine oxidase (MAO) activity was reduced by 47% to 72% in the duodenal mucosa, heart, and brain of Thornber chickens given feed treated with furazolidone for 10 days. MAO activity in the liver was not altered by this treatment. Administration of 200mg/kg furazolidone by crop tube inhibited MAO activities in duodenal mucosa, liver, heart, and brain. Intramuscular administration of 200mg/kg furazolidone did not inhibit MAO activity. Pretreatment with intramuscular neomycin did not antagonize the inhibition of MAO activity by furazolidone (200mg/kg, crop tube). Pretreatment with neomycin by crop tube suppressed the alimentary flora and significantly reduced the effect of furazolidone on MAO activity. This finding suggests that furazolidone is transformed by the alimentary flora to an active metabolite that subsequently inhibits MAO activity in other regions. Furazolidone did not alter aminopyrine demethylase activity in the liver or aspartate transaminase activity in plasma. 20 references. (Author abstract modified)

003712 Allison, J. H.; Boshans, R. L.; Hallcher, L. M.; Packman, P. M.; Sherman, W. R. Sherman: Dept. of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **The effects of lithium on myo-inositol levels in layers of frontal cerebral cortex, in cerebellum, and in corpus callosum of the rat.** Journal of Neurochemistry. 34(2):456-458, 1980.

The effects of lithium on myoinositol levels in layers of frontal cerebral cortex, in cerebellum, and in corpus callosum of the rat were investigated. Lithium lowers myoinositol concentrations to the same degree in layers I through VIA of the frontal cerebral cortex; myoinositol levels in layer VIB and in subcortical white matter were unaltered. Results confirm and extend previous observations that lithium reduces the levels of myoinositol in rat cerebral cortex but not in cerebellum. These results are consistent with the view that the lithium effect on myoinositol is mediated through a muscarinic cholinergic mechanism. 17 references.

003713 Amiragova, M. G.; Stul'nikov, B. V.; Kuksgaus, N. E. Lab. neyroendokrinnoy regulyatsii, Institut normal'noy fiziologii im. P. K. Anokhina, Moskva, USSR /**Thyroxin sensitivity of sensorimotor cortical neurons and the hypothalamic ventromedial nucleus.**/ Chuvstvitel'nost' neyronov sensomotornoy kory i ventro-medial'nogo yadra gipotalamusa k tiroksinu. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova. 66(9):1292-1297, 1980.

Thyroxin sensitivity of sensorimotor cortical neurons and the hypothalamic ventromedial nucleus was studied in 25 alert rabbits using thyroxin microionophoresis without general anesthesia and without muscle relaxation. The activity of the neurons was recorded extracellularly. Using novocaine, openings were made in the skull over the portions of the brain to be studied. The firm brain membrane was removed, and thorough hemostasis was performed. The openings were filled with an agar solution. Using the coordinates of the Sowyer atlas, four channel Pyrex microelectrodes were introduced into the area of the sensorimotor cortex and the hypothalamic ventromedial nucleus. During registration of neuronal activity one of the channels was filled with a solution of NaCl. The other channels were filled with thyroxin. Using a physiological solution and NaOH the pH was brought to 9.5. Results show different sensitivity of these structures to thyroxin. 20 references. (Journal abstract modified)

003714 Andoh, Ryuichiro; Shima, Keisetsu; Miyagawa, Toshiji; Sakurada, Shinobu; Kisara, Kensuke; Ohsawa, Keisuke; Takahashi, Mitsuo. Dept. of Chemical Pharmacology, Tohoku College of Pharmacy, Sendai 983, Japan **Excitatory effects of dihydrocapsaicin on nociceptive neurons in the medial thalamus.** Japanese Journal of Pharmacology. 30(5):599-605, 1980.

The effects of capsaicin and dihydrocapsaicin on single unit activity in the medial thalamus were studied in 32 cats immobilized with gallamine. Of the 56 neurons recorded, 28 were responsive to both noxious and nonnoxious stimuli, 16 were activated only by nonnoxious stimuli, and 12 failed to respond to any natural stimulus. Somatic receptive fields of nociceptive and nonnociceptive neurons were widely distributed over the whole body. Intraarterial administration of bradykinin, capsaicin, or dihydrocapsaicin activated 26 of the 28 nociceptive neurons but only 2 of the 16 nonnociceptive neurons. The increase in firing frequency induced by capsaicin and dihydrocapsaicin was inhibited by morphine; and the morphine inhibition was in turn antagonized by naloxone. Medial thalamic neuronal activity induced by nonnoxious stimuli was not affected by morphine or naloxone. Results suggest that capsaicinoids, like bradykinin, selectively activate pain conducting fibers. 15 references. (Author abstract modified)

003715 Anhut, H.; Knepel, W.; Nutto, D.; Hertting, G. Pharmakologisches Institut der Universitat Freiburg, Hermann-Herder-Strasse 5, D-7800 Freiburg i.Br., West Germany **Vasopressin stimulates release of beta-lipotropin and beta-endorphin in conscious rats as measured by radioimmunoassay of unextracted plasma.** Naunyn-Schmiedeberg's Archives of Pharmacology. 316(1):59-63, 1981.

Arginine vasopressin caused a dose dependent increase in plasma beta-endorphin-like immunoreactivity in male Wistar rats, from 34.5fmol/ml in vehicle treated rats to 205.0fmol/ml after injection of the highest dose of vasopressin (486ng/100g). In view of the cross-reactivity of beta-lipotropin (beta-LPH) in the radioimmunoassay used, plasma was extracted and subjected to gel chromatography. On the average, about 70% of the beta-endorphin-like immunoreactivity coeluted with human beta-LPH and about 30% with human beta-endorphin. Results indicate that vasopressin stimulates beta-LPH and beta-endorphin release into the systemic circulation. 31 references. (Author abstract modified)

003716 Anissimov, J. Z; Deleva, J. I.; Nicolov, N. A.; Sudakov, K. V.; Sherstnev, V. V. Nicolov: Dept. pathophysiclogy, I. G. Soflisky Str., Sofia 1431, Bulgaria **Neuronal sensitivity of some brain regions to Angiotensin II in rabbits.** Agressologie. 21(3):171-175, 1980.

Peculiarities and characteristics of neuronal sensitivity to the microionophoretic introduction of Angiotensin II in the brain cortex, locus coeruleus, and hypothalamus of unanesthetized rabbits were studied. Six typical neuronal reactions to Angiotensin II were observed, including fast and slow activating and inhibiting reactions and phase reactions. Results show that 85% of cortical neurons, 75% of locus coeruleus neurons, and 63% of hypothalamic neurons are sensitive to Angiotensin II. It is thought that peculiarities and sensitivity observed in the neurons which were studied are determined by their functional and neurochemical properties. 32 references. (Journal abstract modified)

003717 Asano, Tomiko; Mizutani, Akira. Dept. of Biochemistry, Institute for Developmental Research, Aichi Prefectural Colony, Kasugai, Aichi 480-03, Japan **Brain benzodiazepine receptors and their rapid changes after seizures in the Mongolian gerbil.** Japanese Journal of Pharmacology. 30(6):783-788, 1980.

The potencies of various benzodiazepines as inhibitors of 3H-diazepam binding to Mongolian gerbil brain membranes correlated closely with their potencies as anticonvulsants. Seizures increased the specific binding of 3H-diazepam to membranes of all regions of the gerbil brain, with the greatest increase in the striatum. The increase was maximal 10 minutes after the seizure, and binding returned to control level within 20 minutes. The increase in specific 3H-diazepam binding was due almost entirely to changes in the affinity of 3H-diazepam for its receptors. 17 references. (Author abstract modified)

003718 Azuma, Haruyoshi; Oshino, Nozomu. Research II, Nihon Schering K. K. 2-6-64, Nishimiyahara, Yodogawa-ku, Osaka 532, Japan **Stimulatory action of lisuride on dopamine-sensitive adenylate cyclase in the rat striatal homogenate.** Japanese Journal of Pharmacology. 30(5):629-639, 1980.

Guanosine triphosphate (GTP) and guanyl-5′-yl imidophosphate significantly potentiated the stimulatory effect of lisuride on dopamine sensitive adenylate-cyclase activity in male Sprague-Dawley rat corpus striatum homogenates. Haloperidol abolished the effect of lisuride. At a concentration above 3mcM, lisuride inhibited stimulation of cyclic AMP formation by dopamine. Results indicate that lisuride, like apomorphine, acts as a partial agonist/antagonist. 31 references. (Author abstract modified)

003719 Baker, G. B.; McKim, H. R.; Coutts, R. T.; Calverley, D. G.; Benderly, A.; Dewhurst, W. G. Neurochemical Research Unit, Dept. of Psychiatry, University of Alberta, Edmonton, Alberta, Canada T6G 2G3 **Interactions between a monofluorinated analogue of p-chloroamphetamine and 5-hydroxytryptamine in brain.** Neuropharmacology. 19(12):1255-1256, 1980.

Interactions between a monofluorinated analogue of p-chloroamphetamine (pCA), 2-amino-1-(4-chlorophenyl)-3-fluoropropane (FpCA), and brain 5-hydroxytryptamine (5-HT) were investigated. Administration of pCA resulted in a marked decrease (54%) of brain 5-HT concentrations after 1.5 hours, and the 5-HT level was depressed still further after 24 hours. The monofluorinated analogue, FpCA, caused a significant decrease (24%) of brain 5-HT levels at 1.5 hours, but by 24 hours, 5-HT had returned to control values. It is suggested that FpCa may be a useful pharmacological tool for the study of processes such as tryptophan hydroxylase activity. 8 references.

003720 Bannet, Jacob; Gillis, Samuel; Ebstein, Richard P.; Belmaker, Robert H. Belmaker: Jerusalem Mental Health Center - Ezrath Nashim, P.O. Box 140, Jerusalem, Israel **Effect of chronic sulpiride on striatal spiperone binding.** International Pharmacopsychiatry. 15(6):334-337, 1980.

The effect of chronic sulpiride was compared to that of chronic haloperidol on striatal 3H-spiperone binding in rats. Increased 3H-spiperone binding after chronic neuroleptic treatment has been proposed as a molecular model of tardive dyskinesia. Three weeks of haloperidol feeding caused a 28% increase in 3H-spiperone binding, whereas even very high dose sulpiride had no effect on spiperone binding. These findings support the concept that sulpiride may be a unique neuroleptic with regard to long-term effects on dopamine receptors. 15 references. (Author abstract modified)

003721 Bar, P. R.; Gispen, Willem H.; Isaacson, Robert L. Isaacson: Dept. of Psychology, SUNY, Binghamton, NY 13901 **Behavioral and regional neurochemical sequelae of hippocampal destruction in the rat.** Pharmacology Biochemistry and Behavior. 14(3):305-312, 1981.

Endogenous in vitro protein phosphorylation was measured in membranes obtained from the nucleus accumbens, nucleus caudatus, septal area, hypothalamus, and frontal neocortex of male Wistar rats 8 and 28 days after bilateral hippocampal lesions, damage limited to the posterolateral neocortex, or sham operations. Membrane protein profiles measured by sodium dodecyl sulphate polyacrylamide slab gel electrophoresis from tissue obtained from all groups were remarkably similar, as were the phosphoprotein profiles. The most prominent bands for phosphoprotein activity had estimated molecular weights of 43K, 48K, 50K, and 82K dalton. Endogenous phosphorylation was enhanced in the caudate and accumbens samples 8 days after hippocampal destruction, but samples from these areas in cortically lesioned animals did not differ from control samples. Both groups of lesioned animals had enhanced endogenous phosphorylation of membrane proteins in caudate and accumbens samples 28 days after surgery, compared to controls. Changes were also found in neocortical samples. Animals with hippocampal destruction tended to groom less than other animals at both postoperative periods, but did not differ from the other animals when tested for excessive grooming after water immersion. 47 references. (Author abstract modified)

003722 Barbeau, H.; Bedard, P. Dept. of Anatomy, Laval University, Centre de recherche en neurobiologie, Hopital de l'Enfant Jesus, 140, 18e Rue Quebec G1J 1Z4, Canada **Denervation supersensitivity to 5-hydroxytryptophan in rats following spinal transection and 5,7-dihydroxytryptamine injection.** Neuropharmacology. 20(6):611-616, 1981.

Within 3 days after transection of the spinal cord in female Wistar rats, a single injection of 5-hydroxytryptophan (5-HTP) or quipazine induced a small increase in the spontaneous electromyographic (EMG) activity in the paralyzed hindlimbs. The amplitude of the response increased with time and reached a maximum 30 days after transection. The amplitude of the flexor contraction in response to electrical stimulation of the paw also increased progressively after transection. When transection was performed 20 days after intraventricular injection of 5,7-dihydroxytryptamine, 5-HTP markedly increased the spontaneous level of EMG activity in the hindlimbs 1 day after transection, but did not significantly modify the flexor response. Results suggest that specific supersensitivity to serotonin develops after spinal cord transection. 13 references. (Author abstract modified)

003723 Barkai, Amiram I. Dept. of Psychiatry, Columbia University College of Physicians and Surgeons, 722 West 168th St., New York, NY 10032 **Myo-inositol turnover in the intact rat brain: increased production after d-amphetamine.** Journal of Neurochemistry. 36(4):1485-1491, 1981.

Apparent turnover of myo-inositol in the brain of urethane anesthetized rats was estimated in vivo from the rate of appearance of endogenous myo-inositol in the cerebroventricular compartment. Ventricular-cisternal perfusion technique combined with isotope dilution of (14C)myo-inositol was used to determine the rate of appearance of brain produced myo-inositol and its modification by d-amphetamine. A mean value of 0.75 nmol/min was obtained for the rate of appearance in the cerebroventricular system. A dose dependent increase in this rate was seen after the administration of d-amphetamine. The endogenous removal of myo-inositol from the perfusate was also studied and found to be mediated in part by a saturable transport system that was not influenced by d-amphetamine. The rate of entry of myo-inositol from blood to the cerebroventricular system was very low and accounted for only 2% of the total rate of appearance, indicating that the majority of myo-inositol in the rat cerebroventricular fluid originates in the brain. 30 references. (Author abstract modified)

003724 Barondes, Samuel H. Dept. of Psychiatry, University of California, San Diego, La Jolla, CA 92093 **Developmentally regulated lectins in slime moulds and chick tissues – are they cell-adhesion molecules?** In: Curtis, A., Cell adhesion and motility. Cambridge, MA, Cambridge University Press, 1980. (p. 309-328).

Approaches to the identification of cell adhesion molecules are considered, and studies of lectins in cellular slime molds and chick tissues which implicate them as possible cell adhesion molecules are reviewed. There is considerable evidence that the lectins in slime molds play a role in cell-cell adhesion. Four out of five criteria are met and failure to consistently meet the fifth criterion could be a false negative. Much less is known about the lectins in developing and adult chick tissue: however, some evidence is consistent with their role in cell-cell or cell-matrix interactions. There is a distinct possibility that the same lectin functions differently in different tissues and at different stages of development. 26 references.

003725 Basseches, P. J.; DiGregorio, G. J. Hahnemann Medical College, Hospital of Philadelphia, 245 North 15th St., Philadelphia, PA 19102 **Quantitation and comparison of phenobarbital levels in the plasma, saliva, and cerebrospinal fluid of the rat, and the demonstration of an alteration of drug passage by ethanol.** Drug and Alcohol Dependence. 5:305-310, 1980.

The ability and extent of three biological fluids (plasma, saliva, and cerebrospinal fluid) to compartmentalize intravenously administered phenobarbital was examined and was correlated. The three fluid compartments showed markedly different levels of phenobarbital, although this probably did not reflect qualitative differences in the barriers that separate them, but rather in the nature of the compartments themselves. Intravenous administration of 400mg/kg ethanol following the intravenous administration of 20mg/kg phenobarbital was shown to alter the passage of phenobarbital into the different fluid compartments, causing a significant increase in the phenobarbital level of cerebrospinal fluid as compared to controls receiving no ethanol. Although the effect seen in the cerebrospinal fluid was significant and the effect in saliva was not significant, it is concluded that the action of ethanol in altering drug passage is a nonspecific effect on the vasculature. This finding of altered drug passage helps explain the observed synergistic interaction of ethanol and various sedative drugs. (Journal abstract modified)

003726 Baudry, Michel; Lynch, Gary. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Characterization of two (3H)glutamate binding sites in rat hippocampal membranes.** Journal of Neurochemistry. 36(3):811-820, 1981.

The specific binding of L-3H-glutamate to Sprague-Dawley rat hippocampal membranes was inhibited by low concentrations of sodium (0.5 to 5.0mM), but was stimulated by higher concentrations (10 to 150mM). The relative potencies of various compounds as inhibitors of L-3H-glutamate binding suggested that sodium independent binding sites were related to postsynaptic glutamate receptors and that sodium dependent sites were related to high affinity uptake sites. The regional distribution of the sodium dependent site varied considerably in parallel with that of high affinity glutamate uptake. The sodium independent binding site showed less regional variation. 31 references. (Author abstract modified)

003727 Behbehani, M. M. Dept. of Physiology, University of Cincinnati, College of Medicine, 231 Betheada Ave., Cincinnati, OH 45267 **Effect of chronic morphine treatment on the interaction between the periaqueductal grey and the nucleus raphe magnus of the rat.** Neuropharmacology. 20(6):581-586, 1981.

Injection of glutamate into the periaqueductal grey (PAG) of Sprague-Dawley rats increased the firing rate of cells in the PAG and nucleus raphe magnus (NRM) and produced analgesia. In morphine tolerant animals, the response of NRM cells to microinjection of glutamate into the PAG was reduced significantly. After naloxone was iontophoresed into the NRM, there was a small increase in the spontaneous firing rate and glutamate produced a significant increase in NRM cell firing rate. It is concluded that chronic morphine treatment decreased the effectiveness of excitation of cells in the PAG in activating NRM cells. This process may be involved in the development of tolerance to the analgesic effect of morphine. 40 references. (Author abstract modified)

003728 Benardo, Larry S.; Prince, David A. Prince: Dept. of Neurology, Stanford University School of Medicine, Stanford, CA 94305 **Acetylcholine induced modulation of hippocampal pyramidal neurons.** Brain Research. 211(1):227-234, 1981.

In guinea-pig hippocampal slices maintained in vitro, acetylcholine (ACh) induced slow depolarizations and simultaneous increases in membrane resistance (RN) in pyramidal neurons. Increases in RN had voltage dependent as well as voltage independent components. These effects were associated with increases in cell discharge frequency and the development of spontaneous and evoked burst discharges. Muscarinic antagonists blocked these actions and produced a decrease in membrane resistance, which appeared to be due to blockade of a tonic effect of ACh on postsynaptic membrane properties. Results suggest that ACh acts as a neuromodulator in the hippocampus. 36 references. (Author abstract modified)

003729 Bendek, G.; Hahn, Z. Institute of Physiology, University Medical School, Szigeti u. 12, Pecs, H-7643, Hungary **Effect of amphetamine on the metabolism and incorporation of (3H)-thymidine into DNA of developing rat brain.** Developmental Neuroscience. 4(1):55-65, 1981.

The effect of amphetamine on the metabolism and incorporation of (3H)-thymidine into DNA of developing rat brain was investigated. High doses of dl-amphetamine inhibited the cell proliferation in the forebrain of 10-day-old rats 2 hours after treatment, in terms of the incorporation of (3H)-thymidine into DNA. The relative specific radioactivity of DNA was decreased to 70% compared to controls. The norepinephrine level of the forebrain was reduced to 30% to 50% of the control value. The observed elevation of plasma corticosterone level did not appear to mediate the effect on cell proliferation. Kinetic studies indicated that the entry of precursor from the blood to the brain tissue was enhanced, but the higher tissue concentration of precursor was not utilized in the DNA synthesis with the same speed. DNA synthesis in the cerebellum was not suppressed by amphetamine treatment. The possible connection between the change in norepinephrine pools and the proliferative activity is considered. 40 references. (Author abstract modified)

003730 Benzi, G.; Arrigoni, E.; Dagani, F.; Marzatico, F.; Curti, D.; Raimondo, S.; Dossena, M.; Polgatti, M.; Villa, R. F. Dept. of Science, Institute of Pharmacology, University of Pavia, Pavia, Italy **Age-dependent modification of drug interference on the enzymatic activities of the rat brain.** Experimental Gerontology. 15(6):593-603, 1980.

Age dependent and drug dependent changes of some cerebral enzyme activities (lactate dehydrogenase, citrate synthase, and malate dehydrogenase, total NADH-cytochrome-c reductase, and cytochrome oxidase) were studied in the homogenate in toto and/or in the crude mitochondrial fraction of the brains of 20-week-old, 60-week-old, 100-week-old, and 140-week-old rats. Enzyme activities decreased consistently with age. The effects of trimetazidine, papaverine, vincamine, theophylline, nicergoline, and cytidine diphosphate choline on enzyme activities were assessed. Drug interference with enzyme activities was found to decrease with age. 28 references. (Author abstract modified)

003731 Besser, G. M.; Delitala, G.; Grossman, Ashley; Stubbs, W. A.; Yeo, T. Dept. of Endocrinology, St. Bartholomew's Hospital, London, EC1A 7BE, England **Chlorpromazine, haloperidol, metoclopramide and domperidone release prolactin through dopamine antagonism at low concentrations but paradoxically inhibit prolactin release at high concentrations.** British Journal of Pharmacology. 71(2):569-573, 1980.

Low concentrations of chlorpromazine, haloperidol, metoclopramide, and domperidone antagonized the dopamine mediated inhibition of prolactin release from perfused columns of dispersed female Wistar rat anterior pituitary cells. All four drugs were less effective as dopamine antagonists at higher concentrations. In the absence of dopamine, high concentrations of chlorpromazine, haloperidol, metoclopramide, and domperidone paradoxically suppressed prolactin secretion. 25 references. (Author abstract modified)

003732 Besser, G. M.; Delitala, G.; Grossman, A.; Yeo, T. Dept. of Endocrinology, St. Bartholomew's Hospital, West Smithfield, London, EC1A 7BE, England **Metergoline and cyproheptadine suppress prolactin release by a non-5-hydroxytryptaminergic, non-dopaminergic mechanism.** British Journal of Pharmacology. 70(1):5-7, 1980.

Cyproheptadine and metergoline were investigated and were both found to be potent inhibitors of prolactin secretion in a dispersed anterior pituitary cell system from female Wistar rats. However, the inhibition was not antagonized by 5-hydroxytryptamine or by a variety of dopaminergic agonists. Results indicate that both drugs act through mechanisms that are neither serotonergic nor dopaminergic. 10 references. (Author abstract modified)

003733 Binek, Patricia A.; Johnson, Terry C.; Kelly, Chester J. Johnson: Division of Biology, Kansas State University, Manhattan, KS 66506 **Effect of alpha-methylphenylalanine and phenylalanine on brain polyribosomes and protein synthesis.** Journal of Neurochemistry. 36(4):1476-1484, 1981.

The effect of alpha-methylphenylalanine and phenylalanine on brain polyribosomes and protein synthesis was assessed. Chronic hyperphenylalanemia was effectively produced in developing mice by daily administration of phenylalanine and a phenylalanine hydroxylase inhibitor alpha-methyl-D,L-phenylalanine. The presence of alpha-methylphenylalanine in newborn mice inhibited 65% to 70% of hepatic phenylalanine hydroxylase activity within 12 hours. Since this maximum inhibition persisted for 24 hours or longer, decreased enzyme activity was maintained by daily administrations. Whereas concentrations of phenylalanine increase approximately 40 fold in both plasma and brain following injection of alpha-methylphenylalanine and phenylalanine, plasma levels of tyrosine were not altered significantly. In addition to polyribosomes disaggregation, chronic hyperphenylalanemia reduced the rates of polypeptide chain elongation on polyribosomes isolated from brain homogenates. 38 references. (Author abstract modified)

003734 Bizzini, B.; Grob, P.; Akert, K. Akert: Brain Research Institute, University of Zurich, August Forelstrasse 1, CH-8029 Zurich, Switzerland **Papain-derived fragment IIc tetanus toxin: its binding to isolated synaptic membranes and retrograde axonal transport.** Brain Research. 210(1-2):291-299, 1981.

The transport characteristics and synaptic membrane binding of the papain derived fragment IIc of tetanus toxin were studied. Like the immunologically identical B-IIb fragment, the IIc fragment was able to bind to male Sprague-Dawley rat isolated synaptic membranes and to be transported retrogradely from axonal endings within muscle to the motoneuronal perikarya in female Sprague-Dawley rats. It is concluded that fragment IIc may serve as a specific carrier for chemical and chemotherapeutic agents into the CNS. 24 references. (Author abstract modified)

003735 Bloom, F. E.; Magistretti, P. J.; Shoemaker, W. J.; Siggins, G. R.; Staunton, D. A. Arthur Vining Davis Center for Behavioral Neurobiology, Salk Institute, La Jolla, CA **Pharmacological bases of psychoneuroendocrinology: preclinical assessment of clinical facts.** In: Brambilla, F., ed., Progress in psychoneuroendocrinology. New York, Elsevier/North Holland, 1980. 669 p. (p. 127-134)

Binding assays and single cell recording techniques were used to study the molecular and cellular changes induced by chronic lithium administration to rats. Electrophysiological data indicate that cerebellar Purkinje neurons become supersensitive to exogenous norepinephrine after chronic lithium treatment. In contrast, lithium treatment selectively reduces the affinity of dopamine agonists (but not antagonists) for dopamine receptor sites in the neostriatum. Results are discussed in relation to the use of complementary electrophysiological and neurochemical measurements in the assessment of psychoactive drugs. 29 references.

003736 Bowdler, Julie M.; Green, A. Richard; Rawle, Frances C. University Dept. of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England **Brain and serum calcium concentrations following electroconvulsive shock or bicuculline-induced convulsions in rats.** British Journal of Pharmacology. 71(1):321-325, 1980.

Serum and regional brain calcium concentrations in male Sprague-Dawley rats anesthetized with halothane and given a single electroconvulsive shock (ECS) did not differ markedly from those in anesthetized controls. When five ECS were given over 10 days, no significant changes in serum or brain calcium concentration were observed, except for an increase in the pons medulla. A single convulsion induced by bicuculline (0.375mg/kg i.v.) resulted in a marked increase in calcium concentration in serum but not in brain. Diazepam pretreatment prevented both the convulsion and the serum calcium change. Results are discussed in relation to clinical data on calcium changes following electroconvulsive therapy and the enhanced monoamine mediated behaviors that follow ECS in rats. 12 references. (Author abstract modified)

003737 Bowen, Wayne D.; Gentleman, Susan; Herkenham, Miles; Pert, Candace B. Pert: Biochemistry and Pharmacology Sect., Biological Research Branch, NIMH, Bldg. 10, Room 2N315, 9000 Rockville Pike, Bethesda, MD 20205 **Interconverting mu- and delta-forms of type 1 opiate receptors in rat striatal patches.** Bethesda, MD, NIMH, 1981. 14 p.

The binding of a radiolabeled mu receptor prototype opiate, dihydromorphine (DHM), and a delta receptor prototype D-Ala2-D-leu5-enkephalin (D-ENK), to slide mounted rat caudate slices simultaneously was compared quantitatively and visualized by audioradiography. Divalent ions, Na plus and GTP, caused an increase in D-ENK binding at the expense of DHM binding at striatal opiate receptor patches. This indicates that D-ENK can bind to brain in a distribution pattern identical to that of DHM and naloxone (type 1 pattern). The relative affinity of opiate receptors for opiate peptides, naloxone, and morphine is a function of incubation conditions and is not indicative of distinctly different opiate receptors. A three state allosteric model is posited which consists of mu agonist, mu antagonist, and adenylate/cyclase coupled delta agonist preferring states, whose equilibrium may be regulated by sulfhydryl groups. 38 references. (Author abstract)

003738 Bowers, Malcolm B., Jr.; Rozitis, Angelika. Dept. of Psychiatry, Yale University School of Medicine, 25 Park St., New Haven, CT 06519 **Dopamine metabolites in caudate and cortex after lithium and haloperidol. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-28216, 1980. 5 p.

To further investigate the mechanism by which lithium and neuroleptics complement each other in the treatment of psychotic disorders, the effects of lithium and haloperidol administration on dopamine metabolites in the caudate and cerebral cortex of the rat were studied following acute and chronic treatment with each agent alone and in combination. Concomitant lithium administration was found to enhance the increase in dopamine metabolites in the brain produced by acute haloperidol administration. Although lithium alone did not increase dihydroxyphenylacetic acid or homovanillic acid in the cortex, in combination with haloperidol there was a trend for lithium to enhance metabolite production in this region. Lithium also appeared to counteract the tendency for tolerance in both caudate and cortex following more prolonged administration of haloperidol. 5 references.

003739 Braestrup, C.; Nielsen, M.; Biggio, G.; Squires, R. F. Squires: Lederle Laboratory, Pearl River, NY **Neuronal localization of benzodiazepine receptors in cerebellum.** Neuroscience Letters. 13:219-224, 1979.

The cellular localization of benzodiazepine receptors was studied in rat and mouse cerebellum. Kainic acid-induced neuronal lesions in rat cerebellum decreased specific binding of (3H)flunitrazepam down to 35% of controls. Specific binding of (3H)flunitrazepam was also decreased to 80% of controls in the cerebellum of mutant nervous mouse where Purkinje cells are degenerated but not in the mutant weaver mouse where granule cells are degenerated. Results indicate that benzodiazepine receptors are located mainly on Purkinje cells and other neurons but not to a great extent on granule cells. (Journal abstract modified)

003740 Brantl, Victor; Teschemacher, Hansjorg; Blasig, Julia; Henschen, Agnes; Lottspeich, Friedrich. Max-Planck-Institut fur Psychiatrie, Dept. of Neuropharmacology, Kraepelinstrasse 2, D-8000 Munchen 40, West Germany **Opioid activities of beta-casomorphins.** Life Sciences. 28(17)1903-1909, 1981.

Beta-casomorphin-7 (H-Tyr-Pro-Phe-Pro-Gly-Pro-Ile-OH) and its analogues beta-casomorphin-6, beta-casomorphin-5, and beta-casomorphin-4 (derived by sequential removal of respectively one, two, or three amino acid residues from the C-terminus) were tested for their opioid activities in a variety of assay systems. Each of the four peptides displayed opioid activity in an opiate receptor binding assay, the isolated mouse vas deferens (MVD), the guinea-pig ileum longitudinal muscle myenteric plexus preparation (GPI), and produced naloxone reversible analgesia after intracerebroventricular injection into rats. In contrast, none of the peptides displayed opioid activity in the isolated rat vas deferens preparation (RVD). Beta-casomorphin-5 was the most potent compound in all the assays employed. Each beta-casomorphin was more potent on the GPI than on the MVD. In view of the fact that the GPI, MVD, and RVD are populated predominantly by mu, delta, and epsilon receptors, respectively, the beta-casomorphins probably represent mu type opiate receptor agonists. 17 references. (Author abstract)

003741 Brase, David A. Dept. of Pharmacology, Eastern Virginia Medical School, P. O. Box 1980, Norfolk, VA 23501 **Pre- and postsynaptic striatal dopamine receptors: differential sensitivity to apomorphine inhibition of (3H)dopamine and (14C)GABA release in vitro.** Journal of Pharmacy and Pharmacology. 32(6):432-433, 1981.

A low concentration of apomorphine (25mcM) significantly inhibited the potassium evoked release of 3H-dopamine from male Sprague-Dawley rat striatal slices, but did not significantly alter 14C-GABA release. At 50 and 100mcM, apomorphine produced a similar inhibition of both 3H-dopamine and 14C-GABA. Results suggest that presynaptic dopaminergic autoreceptors on striatal terminals are more sensitive than postsynaptic striatal dopamine receptors to low concentrations of apomorphine. 13 references.

003742 Buckle, P. J.; Spence, I. Spence: Dept. of Pharmacology, University of Sydney, NSW 2006, Australia **The site of action of muscle relaxant purine nucleosides.** Naunyn-Schmiedeberg's Archives of Pharmacology. 316(1):64-68, 1981.

The effects of a series of purine nucleosides on muscle relaxation in conscious male Fullinsdorf mice and on spinal reflexes and neuromuscular transmission in mice anesthetized with pentobarbitone were examined. The marine product 1-methylisoguanosine (5 to 15mcmol/k) and 2-chloroadenosine (1 to 5mcmol/kg) depressed monosynaptic and polysynaptic spinal reflexes, but did not depress neuromuscular transmission except at 300mcmol/kg doses; both compounds caused muscle relaxation in conscious animals. Adenosine and 1-methyladenosine did not produce muscle relaxation and only slightly depressed polysynaptic reflexes. Theophylline enhanced polysynaptic reflexes and antagonized the depression of these reflexes by 1-methylisoguanosine. Adenosine and 1-methylisoguanosine had no affect on the development of tension by isolated diaphragm muscles. Results suggest that 2-chloroadenosine and 1-methylisoguanosine produce their muscle relaxant effects by depressing activity in the CNS. 14 references. (Author abstract modified)

003743 Campbell, J. L.; Sherman, A. D.; Petty, F. Neurochemical Research Labs., Dept. of Psychiatry, University of Iowa College of Medicine, 500 Newton Road, Iowa City, IA 52242 **Diazepam anxiolytic activity in hippocampus.** Communications in Psychopharmacology. 4(5):387-392, 1980.

Diazepam levels in eight rat brain areas were assessed during conflict and learned helplessness paradigms, and the relationships between regional diazepam levels and behavioral effects were studied. A significant correlation between increasing drug level and behavioral effects was found only in the hippocampus, in both paradigms. Diazepam was then injected regionally into the anterior neocortex, lateral geniculate body, and hippocampus, and the effect on learned helplessness was tested. A significant effect on learned helplessness was found only in hippocampus. These data are consistent with a site for anxiolytic activity of diazepam in the hippocampus. These and previous data suggest a GABAergic or noradrenergic effect of diazepam in the hippocampus. 17 references. (Author abstract modified)

003744 Caputi, A. P.; Rossi, F.; Carney, K.; Brezenoff, H. E. Brezenoff: Dept. of Pharmacology, CMDNJ New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 **Modulatory effect of brain acetylcholine on reflex-induced bradycardia and tachycardia in conscious rats.** Journal of Pharmacology and Experimental Therapeutics. 215(2):309-316, 1980.

The effects of i.c.v. injection of physostigmine and hemicholinium-3 (HC-3) on reflex bradycardia and tachycardia have been studied in unanesthetized rats. The reflex increases and decreases in heartrate were elicited by i.v. injection of norepinephrine and sodium nitroprusside, respectively. Physostigmine increased basal mean arterial pressure, reduced basal heartrate, enhanced the reflex bradycardia, and reduced reflex tachycardia, but did not modify either the pressor effect of norepinephrine, the depressor effect of sodium nitroprusside, or the responsiveness of peripheral muscarinic receptors. Injection of HC-3 did not modify mean arterial pressure, but reduced heartrate and inhibited both reflex bradycardia and reflex tachycardia. Results suggest that brain acetylcholine has a modulatory effect on baroreceptor reflexes. This modulation operates through muscarinic receptors in reflex techycardia and through both muscarinic and nicotinic receptors in reflex bradycardia. 33 references. (Author abstract modified)

003745 Cerrito, Franca; Raiteri, Maurizio. Raiteri: Istituto di Farmacologia e Farmacognosia, Universita di Genova, Via Capo S. Chiara 5, I-16146 Genova, Italy **Supersensitivity of central noradrenergic presynaptic autoreceptors following chronic treatment with the antidepressant mianserin.** European Journal of Pharmacology. 70(3):425-426, 1981.

The inhibitory effect of extracellular noradrenaline (NA) on 3H-NA release from hypothalamic synaptosomes was consistently potentiated in preparations from male Wistar rats treated with the antidepressant mianserin (10mg/kg/day i.p.) for 15 days, compared with those from saline treated controls. No potentiation was observed in synaptosomes from animals given a single injection of mianserin. Results indicate that the noradrenergic release system becomes more susceptible to the negative feedback regulatory action of NA after long-term blockade of alpha2-presynaptic receptors. 5 references.

003746 Chang, Kwen-Jen; Killian, Anthony; Hazum, Eli; Cuatrecasas, Pedro; Chang, Jaw-Kang. Dept. of Molecular Biology, Wellcome Research Laboratories, Research Triangle Park, NC 27709 **Morphiceptin (NH4-Tyr-Pro-Phe-Pro-CONH2): a potent and specific agonist for morphine (mu) receptors.** Science. 212(4490):75-77, 1981.

Research findings on the synthetic peptide NH2-Try-Pro-Phe-Pro-CONH2 (morphiceptin), which is the amide of a fragment of the milk protein beta-casein, are reported. Morphiceptin has morphine-like activities and is highly specific for morphine (mu) receptors but not for enkephalin (delta) receptors. It is as active as morphine in the guinea-pig ileum but much less active in the mouse and rat vas deferens. The discovery of this specific morphine receptor ligand substantiates the hypothesis of multiple opiate receptors. The ligand, which may be of physiological significance since a very similar, or identical, activity can be detected in enzymatic digests of beta-casein, may prove useful for further investigation of the functions of opiate receptor subtypes. 17 references. (Author abstract modified)

003747 Chang, Ping-Lung. Dept. of Anatomy, College of Medicine, National Taiwan University, Taipei, Taiwan, Republic of China **Effect of 6-hydroxydopamine on the fine structure of the hamster pineal gland.** Proceedings of the National Science Council, Republic of China. 4(4):369-380, 1980.

The effects of 6-hydroxydopamine (6-OHDA) on the pinealocytes and postganglionic sympathetic adrenergic nerve fibers within the pineal glands of newborn and adult hamsters were studied. In 9-day-old hamsters treated with 6-OHDA, the adrenergic nerve endings began to degenerate. Various stages of degenerated adrenergic nerve endings were detected in 16-day-old treated animals, and these nerve endings completely disappeared in the pineals from 23-day-old treated animals. Some cisternae of the smooth surfaced endoplasmic reticulum (smooth ER) and Golgi vacuoles were greatly dilated in the pinealocytes in treated newborn hamsters. In the pineals from treated adult hamsters, many adrenergic nerve endings were degenerated. Some smooth ER in the pinealocytes also showed dilated profiles. The number of dense cored vesicles was reduced, while the lysosome-like dense bodies were increased in the pinealoctyes from treated newborn and adult hamsters. The weights of pineals were significantly reduced, whereas those of the testes and accessory organs were markedly increased in the treated adult hamsters. Results indicate that on intact sympathetic innervation to the pienal gland is essential for its normal function. 40 references. (Author abstract modified)

003748 Chapin, Robert E.; Breese, George R.; Mueller, Robert A. Mueller: 223 Clinical Sciences Bldg., UNC School of Medicine, Chapel Hill, NC 27514 **Antagonism of ethanol-induced decrease in LH by para-chlorophenylalanine: lack of correlation with altered serotonergic mechanisms.** Pharmacology Biochemistry and Behavior. 14(3):293-298, 1981.

The role of central serotonergic neurons in the ethanol-induced depression of plasma LH was studied in castrated Sprague-Dawley rats. Pretreatment with 400mg/kg para-chlorophenylalanine methylester (PCPA) prevented the plasma LH depression induced by 2.0g/kg ethanol. Lower doses of PCPA did not block the ethanol effect, even though they produced similar reductions in hypothalamic 5-hydroxytryptamine (5-HT). The 5-HT agonist 5-methoxy-N,N-dimethyltryptamine (5-MDMT) depressed LH in a dose dependent manner. Methysergide pretreatment blocked the effects of a submaximal dose of 5-MDMT, but did not prevent the fall in LH induced by ethanol. Electrolytic lesions of the median raphe nucleus did not prevent the ethanol-induced depression of LH. It is concluded that activation of the serotonergic system does not play a major role in the ethanol-induced depression of LH. 41 references. (Author abstract modified)

003749 Chevillard, C.; Mathieu, M. N.; Recommis, D. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Prejunctional actions of piribedil on the isolated kidney of the rabbit: comparison with apomorphine.** British Journal of Pharmacology. 71(2):513-518, 1980.

The effects of piribedil (Pir) and apomorphine on contractile responses and noradrenaline (NA) release evoked by sympathetic nerve stimulation were compared in the isolated kidney of the male New Zealand rabbit. Results indicate that Pir has a complex effect on sympathetic transmission. Pir exerts an emphetamine-like action, causing NA release from postganglionic stores. This releasing effect masks an action on prejunctional inhibitory dopamine receptors. At high doses, Pir has a marked action on postjunctional sites, since it reduces the vasoconstrictor effect of exogenous NA. 12 references. (Author abstract modified)

003750 Chiappinelli, V. A.; Cohen, J. B.; Zigmond, R. E. Dept. of Pharmacology, St. Louis University, School of Medicine, 1402 South Grand Blvd., St. Louis, MO 63104 **The effects of alpha- and beta-neurotoxins from the venoms of various snakes on transmission in autonomic ganglia.** Brain Research. 211(1):107-126, 1981.

The blockade of transmission in ciliary and choroid neurons of pigeon and chicken ciliary ganglia by certain lots of alpha-bungarotoxin (1.2mcM) was shown to be due to postsynaptic action characteristic of alpha-neurotoxins. Alpha-cobratoxin (1.2mcM) and certain lots of alpha-bungarotoxin (1.2mcM) produced a partial blockade of transmission in ciliary neurons of the pigeon ciliary ganglion without altering transmission in choroid neurons. The alpha-neurotoxins erabutoxin-a and erabutoxin-b (1.2mcM) had no effect on transmission in either cell population. None of the alpha-neurotoxins tested had any effect on transmission in the rat superior cervical ganglia or pelvic ganglia. Beta-bungarotoxin produced a complete blockade of transmission in avian ciliary ganglia and rat superior cervical ganglia. Unlike the action of alpha-bungarotoxin, the blockade of ciliary ganglia on transmission by beta-bungarotoxin was irreversible and not prevented by pretreatment with tubocurarine. 33 references. (Author abstract modified)

003751 Chiarotti, M.; Giusti, G. V.; Vigevani, F. Ist, Med, Leg., Universita di Cattania, Roma, Italy **In vivo and in vitro properties of anti-delta9-tetrahydrocannabinol antibody.** Drug and Alcohol Dependence. 5:231-233, 1980.

An immune serum to cannabinoids was produced in rabbits and tested in vitro by immunoprecipitation, hemagglutination, and hemagglutination inhibition tests. In vivo, when passively transferred into mice, it prevented the effect of delta9-tetrahydrocannabinol on the barbiturate sleeping time. (Journal abstract)

003752 Chou, Dorothy T.; Forde, Jesse H.; Hirsh, Kenneth R. Dept. of Physiology, General Foods Corporation, Technical Center, 250 North St., White Plains, NY 10625 **Unit activity in medial thalamus: comparative effects of caffeine and amphetamine.** Journal of Pharmacology and Experimental Therapeutics. 213(3):580-585, 1980.

The effects of caffeine and d-amphetamine sulfate on single unit activity recorded extracellularly from the medial thalamus of chloral hydrate anesthetized female Sprague-Dawley rats were examined. Spontaneous firing rates of medial thalamic neurons were markedly suppressed by caffeine (0.1 to 0.5mg/kg i.v.) and markedly augmented by amphetamine (0.1 to 1mg/kg i.v.). Amphetamine was able to activate medial thalamic neurons during caffeine-induced suppression, and caffeine was able to suppress the amphetamine-induced augmentation of neuronal activity. Results indicate that caffeine and amphetamine have different mechanisms of action, at least in the medial thalamus. Data also suggest that caffeine has different actions in different brain areas and that the medial thalamus may be an important site of action for caffeine-induced arousal. 34 references. (Author abstract modified)

003753 Clements-Jewery, S.; Robson, P. A.; Chidley, L. J. Biochemical Pharmacology Section, Biological Research Dept., Roussel Laboratories Ltd., Swindon, Wiltshire, England **Biochemical investigations into the mode of action of trazodone.** Neuropharmacology. 19(12):1165-1173, 1980.

Biochemical investigations into the mode of action of trazodone, an antidepressant drug with well established clinical efficacy in the treatment of depressive disorders, in addition to a marked anxiolytic activity, are described. In contrast to tricyclic, and certain other antidepressant drugs, trazodone has been shown to have no effects on noradrenaline (NA) reuptake mechanisms. The combination of alpha2 antagonism and NA releasing properties, in the absence of reuptake inhibition, may be associated with the antidepressant activity of this drug, whereas the potent 5-HT antagonist activity may explain the anxiolytic effects. Finally, trazodone has been found to be devoid of muscarinic receptor affinity as measured by (3H)quinuclidinyl benzilate radioreceptor assays in accord with clinical observation of the absence of anticholinergic side-effects. 38 references. (Author abstract modified)

003754 Colboc, O.; Costentin, J. Costentin: U.E.R. de Medecine et de Pharmacie, Lab. de Pharmacodynamie et de Physiologie, 49, Rue du Maulevrier, F-76000 Rouen, France **Evidence for thermoregulatory dopaminergic receptors located in the preopticus medialis nucleus of the rat hypothalamus.** Journal of Pharmacy and Pharmacology. 32(9):624-629, 1980.

Systemic administration of apomorphine induces hypothermia in anesthetized or conscious male Sprague-Dawley rats. This effect was antagonized by systemic injection of haloperidol, but not by domperidone. Injections of apomorphine, dopamine, or d-amphetamine into the preopticus medialis nucleus (POMN) of the hypothalamus also induced hypothermia. Injection of haloperidol into the POMN antagonized the hypothermic effect of systemic injection of apomorphine. Heat lesions of the POMN markedly reduced the hypothermic effect of a systemic injection of apomorphine. Results indicate that dopamine receptors involved in thermoregulation are located in the POMN. This nucleus could be involved in heat stroke and in the malignant neuroleptic syndrome. Blockade of dopamine receptors in this structure may contribute to the malignant neuroleptic syndrome sometimes observed in patients treated with antipsychotic drugs. 27 references. (Author abstract modified)

003755 Collins, J. G.; Roppolo, J. R. Dept. of Anesthesiology, Yale University, School of Medicine, 333 Cedar Street, New Haven, CT 06510 **Effects of pentobarbital and ethanol upon single-neuron activity in the primary somatosensory cortex of the rhesus monkey.** Journal of Pharmacology and Experimental Therapeutics. 213(2):337-345, 1980.

The effects of pentobarbital and ethanol upon neuronal activity in the primary somatosensory cortex of awake, nonparalyzed rhesus monkeys were examined to assess the ability of each drug to modify stimulus representation by those neurons. Using microelectrode recording techniques, single neuron spontaneous and stimulus driven activity was studied in the drug free control state, during slow-wave sleep and after cumulative doses of either pentobarbital or ethanol. Pentabarbital caused a profound, dose dependent decrease in both driven and spontaneous activity at levels of drug well below that used for general anesthesia. In addition to changes in firing frequency, pentobarbital also modified the way in which some cells responded to particular simulus attributes. Results provide evidence that the presence of pentobarbital may significantly alter neuronal responses at doses less than that used for general anesthesia. In constrast, ethanol, although it is also a CNS depressant, caused only small changes in neuronal activity of individual somatosensory cortical cells. 35 references. (Author abstract modified)

003756 Collis, Michael G.; Shepherd, John T. Imperial Chemical Industries Ltd., Pharmaceuticals Div., Mereside, Alderley Park, Macclesfield, Cheshire, S.K. 10, 4TG, England **Interaction of the tricyclic antidepressant amitriptyline with prejunctional alpha and muscarinic receptors in the dog saphenous vein.** Journal of Pharmacology and Experimental Therapeutics. 213(3):616-622, 1980.

The effect of amitriptyline on norepinephrine (NE) release from adrenergic nerve endings was studied, using the dog saphenous vein as a model of the sympathetic neuroeffector junction. Amitriptyline increased the overflow of tritiated NE and decreased that of tritiated 3,4-dihydroxyphenylglycol from preloaded, electrically stimulated strips, indicating amitriptyline inhibited neuronal uptake. However, the increased overflow of 3H-NE caused by amitriptyline also occured when neuronal uptake was blocked by cocaine, but was abolished when prejunctional alpha-receptors were blocked by phentolamine. Amitriptyline attenuated the prejunctional inhibitory action of exogenous NE and antagonized the prejunctional inhibitory action of acetylcholine, but did not alter the prejunctional inhibitory effect of histamine. Thus, amitriptyline can increase the concentration of NE at the neuroeffector junction by blocking neuronal uptake and by interacting with prejunctional alpha-adrenergic and muscarinic receptors. The relevance of these findings to the cardiotoxic effects of amitriptyline are discussed. 238 references. (Author abstract modified)

003757 Comis, S. D.; Pratt, S. R.; Hayward, T. L. Neurocommunications Research Unit, Medical School, Birmingham B15 2TJ, England **The effect of frusemide piretanide and bumetanide on cochlear succinic dehydrogenase.** Neuropharmacology. 20(4):405-407, 1981.

The effects of i.p. injection of the loop diuretics frusemide, piretanide, and bumetanide on cochlear succinic dehydrogenase were studied in pigmented guinea-pigs. All three compounds caused a reduction in the succinic dehydrogenase reaction in stria vascularis and in the organ of Corti. Frusemide and piretanide were more active inhibitors in outer hair cells than in inner hair cells, whereas bumetanide affected all hair cells equally. 3 references. (Author abstract modified)

003758 Consolo, S.; Ladinsky, H.; Forloni, G. L.; Tirelli, A. S.; Garattini, S. Instituto di Ricerche Farmacologiche Mario Negri, Via Eritrea, 62, I-20157 Milan, Italy **Comparison of the effects of the stereoisomers of fenfluramine on the acetylcholine content of rat striatum, hippocampus and nucleus accumbens.** Journal of Pharmacy and Pharmacology. 32(3):201-203, 1980.

The effects of fenfluramine isomers on regional brain acetylcholine (ACh) content were studied in female CD-COBS rats. Neither isomer altered ACh content in the brainstem, but both isomers increased ACh content in the nucleus accumbens and hippocampus. The increases in ACh content in the nucleus accumbens were prvented when serotonin synthesis was blocked by p-chlorophenylalanine. In the striatum, ()-fenfluramine increased ACh content, but (-)-fenfluramine had no effect. The ACh increase induced in the straitum by ()-fenfluramine was summated with the increase in ACh induced by apomorphine and was not prevented by dopamine receptor blockade with pimozide. The effect of apomorphine was blocked by (-)-fenfluramine, and pimozide pretreatment unmasked an increase in striatal ACh induced by (-)-fenfluramine. Results suggest that a population of cholinergic neurons intrinsic to the striatum is under inhibitory serotonergic regulation and independent of inhibitory dopaminergic regulation. 17 references. (Author abstract modified)

003759 Conte-Devolx, B.; Oliver, C.; Giraud, P.; Gillioz, P.; Castanas, E.; Lissitzky, J.-C.; Boudouresque, F.; Millet, Y. Laboratoire de Physiologie, Faculte de Medecine, F-13385 Marseilles Cedex 4, France **Effect of nicotine on in vivo secretion of**

melanocorticotropic hormones in the rat. Life Sciences. 28(9):1067-1073, 1981.

Corticosterone, adrenocorticotropic hormone (ACTH), beta-endorphine, and alpha-melanocyte stimulating hormone (alpha-MSH) were measured in rat plasma by radioimmunossay before and 2, 5, 15, and 30 minutes after an intraperitoneal injection of nicotine. Nicotine induced an increase of plasma corticosterone, ACTH, and beta-endorphin and a decrease of alpha-MSH. Dose response experiments showed an increase of corticosterone, ACTH, and beta-endorphin 15 minutes after 250mcg/kg of nicotine; no response was observed after injection of 100 mcg/kg. The decrease of alpha-MSH was observed 15 minutes after 100, 250, or 500mcg/kg of nicotine. Results suggest that the increase of corticosterone is mediated through ACTH release. 27 references. (Author abstract modified)

003760 Corrigal, William A.; Linseman, Mary Ann; Lucato, RoseMarie; Elliott, Myrnalee. Neurobiology Section, Addiction Research Foundation, 33 Russell St., Toronto, Ontario, Canada M5S 2S1 **Differential tolerance to the effects of morphine on evoked activity in the hippocampal slice.** Life Sciences. 28(14);1613-1620, 1981.

Differential tolerance to the effects of morphine on evoked activity in the hippocampal slice preparation is described. Morphine has been shown to have an excitatory effect on monosynaptically evoked CA1 field potentials of the hippocampal slice manifest as an increase in amplitude of the primay population spike near threshold, and by the appearance of secondary and sometimes additional population spikes in response to a single stimulation. The effects of three concentrations of morphine on this response was studied in hippocampal slices taken from rats chronically treated with morphine or sham pellets. Slices from half of the rats in each treatment group were received in normal medium, the other half in medium containing 0.2 mcM morphine. There was a significant indication of tolerance in the morphine treated rats to the secondary spike effect but not to that of the primary spike. There were no significant differences due to the nature of the receiving medium. 22 references. (Author abstract modified)

003761 Cosgrove, James W.; Clark, Bruce D.; Brown, Ian R. Brown: Dept. of Zoology, Scarborough College, University of Toronto, West Hill, Ontario M1C 1A4, Canada **Effect of intravenous administration of d-lysergic acid diethylamide on subsequent protein synthesis in a cell-free system derived from brain.** Journal of Neurochemistry. 36(3):1037-1045, 1981.

An initiating cell free protein synthesis system derived from brain was used to show that i.v. injection of d-lysergic acid (LSD) to male New Zealand rabbits induced a transient inhibition of translation following a brief stimulatory period. This effect was observed in postribosomal supernatant and microsome fractions. The overall decrease in translation was observed even when the hyperthermia normally induced by LSD was prevented by injection at 4 degrees. Differential effects of LSD on particular proteins were observed only when the hyperthermic as well as behavioral effects of the drug were apparent. 43 references. (Author abstract modified)

003762 Cote, Ila L.; Wilson, W. A. Wilson: Epilepsy Center Research Laboratory, Bldg. 2, Durham V.A. Medical Center, Durham, NC 27705 **Effects of barbiturates on inhibitory and excitatory responses to applied neurotransmitters in Aplysia.** Journal of Pharmacology and Experimental Therapeutics. 214(1):161-165, 1980.

The effects of barbiturates on responses to iontophoretically applied acetylcholine (ACh) and GABA were studied in Aplysia californica. Phenobarbital and pentobarbital depressed chloride dependent inhibitory responses to ACh and GABA. This depression occurred at approximately the same concentrations that attenuate excitatory responses. Potassium dependent inhibitory responses were minimally affected. Inhibitory responses were not enhanced, even at concentrations considerably below those that depressed the responses. Results indicate that barbiturates can attenuate inhibitory responses to neurotransmitters. 15 references. (Author abstract modified)

003763 Crews, F. T.; Smith, C. B. Dept. of Pharmacology, University of Florida Medical School, Gainesville, FL 32610 **The effects of antidepressants on the retention and metabolism of (3H)-norepinephrine in rat brain slices.** Neuropharmacology. 20(4):363-369, 1981.

The retention, deamination, and O-methylation of tritiated norepinephrine (3H-NE)by male Sprague-Dawley rat brain slices were studied in the presence of cocaine, reserpine, and antidepressant drugs. Cocaine, which inhibits neuronal membrane uptake, decreased the deamination and retention of 3H-NE but increased O-methylation. Reserpine, which inhibits vesicular transport and bindings, increased deamination, reduced retention, and did not affect O-methylation of 3H-NE. Low concentrations of desipramine inhibited the retention and deamination of 3H-NE in hypothalamus, brainstem, and parietal cortex, but not in the caudate nucleus; at higher desipramine concentrations, retention 3H-NE was reduced further but deamination was increased in the caudate. Nortriptyline and protriptyline had similar effects, but iprindole did not alter 3H-NE retention. Results indicate that tricyclic antidepressants are not specific selective inhibitors of neuronal membrane transport. 18 references. (Author abstract modified)

003764 Culvenor, A. J.; Jarrott, B. Austin Hospital, Heidelberg, Victoria, Australia **Reduction in the level of immunotitratable dopamine beta-hydroxylase after chronic administration of L-Dopa or alpha-methyldopa.** Neuroscience. 4:1381-1389, 1979.

The effect of chronic administration for 7 days of L-DOPA or L-alpha-methyldopa on the activity of dopamine beta-hydroxylase in rat adrenal glands and heart was studied. Both drugs reduced adrenal dopamine beta-hydroxylase activity by 35% whereas only alpha-methyldopa administration lowered enzyme activity in the heart. Immunotitration of rat adrenal supernatants with a specific antibody raised to dopamine beta-hydroxylase purified from bovine adrenal medulla showed that the reductions in adrenal enzyme activity following L-DOPA and alpha-methyl-dopa were due to decreases in the amount of dopamine beta-hydroxylase protein. Chronic administration of L-DOPA did not alter the turnover of trichloracetic acid precipitable soluble protein in the adrenal glands or the heart. Heart tyrosine hydroxylase activity was slightly elevated by chronic administration of alpha-methyldopa, but this dosage regimen considerably reduced both adrenal and heart aromatic L-amino acid decarboxylase activity and slightly decreased the activity of the cytoplasmic marker, lactate dehydrogenase, in adrenal glands. The results are consistent with previous proposals that catecholamine levels may contribute to the regulation of the total amount of dopamine beta-hydroxylase in the peripheral nervous system and that the amounts of catecholamine synthesizing and degrading enzymes are regulated in response to transmitter demand. (Journal abstract modified)

003765 Cvejic, Vesna; Mrsulja, B. B. Mrsulja: Institute of Biochemistry, Faculty of Medicine, Visegradska 26, 11000 Belgrade, Yugoslavia **Catecholamine turnover in rat cerebral cortex and caudate following repeated treatment with dihydroergotoxine.** Gerontology. 27(1,2):7-12, 1981.

The turnover rate of catecholamine in the cerebral cortex and caudate of adult Wistar rats was estimated after inhibition of synthesis by means of alpha-methyl-rho-tyrosine in animals treated with dihydroergotoxine (DHET) for 1, 3, and 10 days. Following single as well as repeated treatments with the drug, blockade of norepinephrine receptors, as indicated by the increased catecholamine turnover rate, was found in both brain structures. The turnover rate of dopamine was changed only after repeated treatments. The turnover rate was decreased in the cortex and increased in the caudate, indicating both agonistic and antagonistic effects of DHET on dopamine receptors. The therapeutic use of DHET is advocated in cerebrovascular insufficiency and geriatric patients. 22 references. (Author abstract modified)

003766 Daly, John W.; Bruns, Robert F.; Snyder, S. H. Laboratory of Bioorganic Chemistry, NIAMDD, NIH, Bethesda, MD 20205 **Adenosine receptors in the central nervous system: relationship to the central actions of methylxanthines.** Life Sciences. 28(19):2083-2097, 1981.

The role of central adenosine receptors in the action of alkylxanthines is reviewed. Adenosine and adenosine analogues have marked behavioral depressant effects. Adenosine reduces spontaneous neuronal activity and inhibits transsynaptic potentials via interaction with extracellular receptors. Adenosine inhibits adenylate cyclase via a high affinity receptor and activates adenylate cyclase via a low affinity receptor. The behavioral, electrophysiological, and biochemical effects of alkylxanthines are consistent with the hypothesis that the central stimulatory actions of caffeine and theophylline are due to antagonism of central adenosine receptors. 124 references. (Author abstract modified)

003767 Davis, Alan; Madras, Bertha; Seeman, Philip. Dept. of Psychopharmacology, Clarke Institute of Psychiatry, 250 College St., University of Toronto, Toronto, Ontario M5T 1R8, Canada **Solubilization of neuroleptic/dopamine receptors of human brain striatum.** European Journal of Pharmacology. 70(3):321-329, 1981.

Dopaminergic neuroleptic receptors were solubilized by digitonin from postmortem human putamen. The receptors were labeled by 3H-spiperone and separated from free 3H-spiperone by sephadex chromatography. The inhibitory and stereoselective potencies of neuroleptics and neurotransmitters on solubilized receptors were similar to those on intact membrane receptors. The dissociation constant for 3H-spiperone was higher in solubilized receptors than in intact membrane receptors, and the density of 3H-spiperone binding sites was lower in soluble material than in intact membranes. Results indicate that the human putamen, unlike the rat striatum, can be solubilized to release neuroleptic dopaminergic receptors. 29 references. (Author abstract modified)

003768 Davis, Leonard G.; Cohen, Ronald K. Missouri Institute of Psychiatry, University of Missouri-Columbia, School of Medicine, 5400 Arsenal St., St. Louis, MO 63139 **Inhibition of (3H)diazepam binding by an endogenous fraction from rat brain synaptosomes.** Journal of Pharmacy and Pharmacology. 32(3):218-219, 1980.

The binding of 3H-diazepam was inhibited by an endogenous fraction from rat brain. Since the endogenous inhibitor was isolated from membrane fractions enriched in benzodiazepine receptors, it may be an endogenous benzodiazepine receptor ligand. Preliminary attempts to identify the endogenous inhibitor showed that its physical properties differ from those of previously reported diazepam ligands. 13 references.

003769 Debus, G.; Kehr, W. Forsch. Laboratories, Schering AG, Berlin, West Germany **Catecholamine and 5-hydroxytryptamine synthesis and metabolism following intracerebroventricular injection of dibutyryl cyclic AMP.** Journal of Neural Transmission. 45:195-206, 1979.

Catecholamine and 5-hydroxytryptamine synthesis and metabolism were measured in the rat in vivo following intracerebroventricular injection of dibutyryl cyclic AMP (cAMP) or dibutyryl cGMP. Dibutyryl cAMP: 1) increased the accumulation of dopa in all brain regions by 70% to 130%; 2) stimulated the formation of 5-hydroxytryptophan in the dopamine rich part of the limbic system, as did dibutyryl cGMP; 3) increased 5-hydroxytryptophan in C. striatum and cerebellum; 4) decreased the noradrenaline level of the C. striatum in a dose dependent manner; and 5) elevated the level of 5-hydroxtryptamine in the brainstem and the level of 5-hydroxyindole acetic acid in the diencephalon and the limbic system. The disappearance of noradrenaline but not of dopamine after inhibition of catecholamine synthesis with alpha-methyl-p-tyrosine methylester HCl was accelerated in most brain regions. The data are compatible with the view that dibutyryl cAMP stimulates tyrosine and tryptophan hydroxylase directly. In addition, dibutyryl cAMP appears to enhance the utilization of noradrenaline but not that of dopamine. The increased utilization of 5-hydroxytryptamine may be restricted to the diencephalon and to the limbic system. (Journal abstract modified)

003770 Degtyarev, V. P. Kafedra normal'noy fiziologii, Moskovskiy meditsinskiy stomatologicheskiy institut im. N. A. Semashko, Moskva, USSR /**The effect of cholinergic substances on nociceptive evoked responses in specific nuclei of the thalamus.**/ Vliyaniye kholinergicheskikh veshchestv na notsitseptivnyye vyzvannyye otvety v spetsificheskikh yadrakh talamusa. Farmakologiya i Toksikologiya. 43(4):360-363, 1980.

The effect of microinjections into the rabbit thalamus (VPM and VPL) of M-cholinomimetic arecoline, M-cholinolytic metamizil, n-cholinomimetic lobeline, and n-cholinolytic beta-ethylenespasmolytin on the formation of nociceptive responses induced by dental pulp stimulation was studied. Results show that: arecoline and beta-ethylenespasmolytin decreased, while metamizil and lobeline increased the amplitude of the primary responses; there were no changes in the latent periods. These results show that the activation of the M-cholinergic structures of specific thalamic nuclei reduces the nociceptive responses, and the activation of the N-cholinergic structures potentiates the nociceptive responses in specific relays. 36 references. (Journal abstract modified)

003771 DeMet, Edward M.; Vosmer, Georgetta; Halaris, Angelos E. Halaris: Veterans Administration Hospital Brentwood, 11301 Wilshire Blvd., Los Angeles, CA 90073 **Noncompetitive amine uptake inhibition by the new antidepressant pridefine.** Journal of Neurochemistry. 36(3):917-923, 1981.

Amine uptake inhibition by pridefine, a new antidepressant, was studied in synaptosomes of male Sprague-Dawley rat frontal cortex, hypothalamus, and striatum. Ouabain controls were used to distinguish passive uptake from active uptake and to resolve passive uptake into its bindings and diffusive elements. Kinetic analyses of the active component indicated the inhibition was noncompetitive, unlike that of tricyclic antidepressants. Pridefine was a relatively specific catecholamine uptake inhibitor and was much weaker as a 5-hydroxytryptamine uptake blocker. 25 references. (Author abstract modified)

003772 Dhumal, V. R.; Gulati, O. D.; Bhavsar, V. H. Dept. of Pharmacology, Government Medical College, Surat and Medical College, Baroda, India **Central hypotensive effect of gamma-**

aminobutyric acid in anaesthetized dogs. Journal of Pharmacy and Pharmacology. 32(10):724-725, 1980.

Intraventricular administration of GABA-induced hypotension and increased the level of noradrenaline (NA) in cerebrospinal fluid in anesthetized mongrel dogs. The hypotensive effect of GABA was antagonized by reserpine and cocaine. Results suggest that the hypotensive effect of GABA is due to release of endogenous NA. 10 references.

003773 Difny, N.; Burks, T. F. Dept. of Neurobiology and Anatomy, University of Texas Medical School at Houston, Houston, TX 77025 **Selective modification by opiates of neuronal activity of the medial basal hypothalamus.** Experimental Neurology. 72(1):1-11, 1981.

The selective modification by opiates of neuronal activity of the medial basal hypothalamus (MBH) was studied in freely behaving rats previously implanted with permanent Nichrome electrodes. Each incremental dose of morphine elicited additional alterations of multiunits. MBH neurons were identified and classified with respect to the response patterns induced by morphine and its antagonist, naloxone. Four patterns (increase, decrease, biphasic change in firing rates, or no effect) of response to morphine and three to naloxone (reversal, no effect, sensitivity to naloxone but not to morphine) were identified. It was observed that only the decreases of firing produced by morphine were blocked by naloxone. 50 references. (Author abstract modified)

003774 Divakaran, P.; Rigor, B. M.; Wiggins, R. C. Dept. of Neurobiology and Anatomy, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **Halothane accumulation in rat brain and liver.** Neurochemical Research. 6(1):77-85, 1981.

Halothane concentrations were measured in rat brain and liver after exposure to various concentrations of halothane in air. Tissue concentrations of halothane were not linearly related to ambient concentrations. An increase in inspired concentration from 1.0 to 1.5% produced little increase in halothane concentration in brain, but liver halothane concentration increased in proportion to the dose increase. With inspired halothane concentrations below 0.5%, tissue concentrations were lower than expected. Body size significantly affected the time required for each tissue to reach equilibrium at a given inspired concentration. Results indicate that tissue concentrations at low exposure levels may be less than proportional to dose and that concentrations in small laboratory animals may be expected to exceed values in humans under equivalent exposure conditions. 13 references. (Author abstract modified)

003775 Doogan, D. P. Dept. of Clinical Research, Philips-Duphar, BV, Weesp, The Netherlands **Fluvoxamine as an antidepressant drug.** Neuropharmacology. 19(12):1215-1216, 1980.

The utility of fluvoxamine, one of the family of aminoethyl oximethers of aralkyl ketones, as an antidepressant drug, is described. In view of the specificity of the drug in affecting 5-hydroxytryptamine metabolism and its lack of pharmacologically active metabolites, fluvoxamine is adjudged a potentially effective antidepressant and a potentially important research tool. It is noted that the indoleamine hypothesis of depression can be examined by investigating the pharmacological effects of this drug and relating them to either clinical or biochemical variables. 6 references.

003776 Dowling, John E.; Watling, Keith J. Watling: Biological Laboratories, Harvard University, Cambridge, MA 02138 **Dopaminergic mechanisms in the teleost retina. II. Factors affecting the accumulation of cyclic AMP in pieces of intact carp retina.** Journal of Neurochemistry. 36(2):569-579, 1981.

The ability of dopamine agonists, other proposed retinal transmitters, depolarizing agents, and light to stimulate adenylate cyclase activity in pieces of intact carp retina was examined. Results indicate that dopamine sensitive adenylate-cyclase is the only neurotransmitter activated adenylate-cyclase in the carp retina. Only dopamine or dopamine agonists stimulated cyclic AMP synthesis in the retina. Depolarizing agents increased retinal cyclic AMP levels, but acted by releasing endogenous stores of dopamine. Retinal cyclic AMP levels were increased by flashing lights or high potassium concentrations, but the increases were abolished by haloperidol. 21 references. (Author abstract modified)

003777 Dubocovich, Margarita L.; Langer, S. Z. Biology Dept. Synthelabo, (L.E.R.S.) 58, rue de la Glaciere, F-75013 Paris, France **Pharmacological differentiation of presynaptic inhibitory alpha-adrenoceptors and opiate receptors in the cat nictitating membrane.** British Journal of Pharmacology. 70(3):383-393, 1980.

The effects of morphine, endogenous opioid peptides, and some synthetic analogues on 3H-noradrenaline release induced by nerve stimulation was studied in the isolated nerve terminal muscle preparation of the cat nictitating membrane under conditions in which the alpha-presynaptic receptors were blocked by phentolamine. Morphine, (Met5)-enkephalin, (Leu5)-enkephalin, and beta-endorphin reduced 3H-noradrenaline overflow and responses to nerve stimulation from the nictitating membrane. These effects were completely antagonized by naloxone. Two synthetic opiate pentapeptides that are resistant to enzymatic degradation were more potent than the enkephalins in reducing the stimulation evoked transmitter overflow. In the presence of 1mdM phenoxybenzamine, 3H-noradrenaline overflow was increased 8 fold, but the inhibition of neurotransmission by methionine-enkephalin was not affected; at 10mcM phenoxybenzamine, 3H-noradrenaline overflow increased 15 fold and the effects of methionine were antagonized. 45 references. (Author abstract modified)

003778 Duggan, A. W.; Griersmith, Bernadette T.; Johnson, S. M. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, Australia **Supraspinal inhibition of the excitation of dorsal horn neurones by impulses in unmyelinated primary afferents: lack of effect by strychnine and bicuculline.** Brain Research. 210(1-2):231-241, 1981.

Tonic descending inhibition of the excitation of lumbar dorsal horn neurons by impulses in unmyelinated primary afferents was measured in barbiturate anesthetized cats by reversibly cooling a more cephalic segment. Supraspinal inhibition was not reduced by bicuculline and strychnine administered i.v. or electrophoretically in the substantia gelatinosa and at sites progressively closer to cell bodies in amounts adequate to reduce segmental inhibition. Results suggest that descending fibers that tonically control spinal transmission of nociceptive information do not release glycine or GABA or excite spinal interneurons that release these amino acids. 19 references. (Author abstract modified)

003779 Dun, N. J.; Karczmar, A. G. Dept. of Pharmacology and Exper. Therapeutics, Loyola University Stritch School of Medicine, 2160 S. First Ave., Maywood, IL 60153 **A comparative study of the pharmacological properties of the positive potential recorded from the superior cervical ganglia of several species.** Journal of Pharmacology and Experimental Therapeutics. 215(2):455-460, 1980.

A comparative study of the pharmacological properties of the positive potential recorded from the superior cervical ganglia (SCG) of several species is described. In curarized guinea-pig SCG, a late negative response (LN) with no detectable slow positive (P) potential was observed. Neostigmine increased the amplitude and duration of the P and LN responses in the majority of the rabbit, rat, and cat SCGs. Alpha-receptor antagonists, phenoxybenzamine, phentolamine, and dihydroergotamine, and a beta-receptor antagonist, propranolol, did not appreciably alter the P and LN responses of the rabbit, cat, and rat SCG or neostigmine-induced hyperpolarization of the guinea-pig SCG. These and other data demonstrate that muscarinic receptors are involved in the generation of P and LN potentials of mammalian sympathetic ganglia, while the adrenergic and disynaptic nature of P response remains to be clarified. There appears to be no correlation between the generation of P potential and elevation of cyclic AMP in the SCG. 29 references. (Author abstract modified)

003780 Dzhokhadze, L. D.; Samadashvili, Z. V. no address / **The effect of Nootropile on the transcallosal and primary evoked responses of the cat cerebral cortex.**/ Vliyaniye Nootropila na vyzvannyye transkallozal'nyye i pervichnyye otvety kory bol'shikh polushariy golovnogo mozga koshek. Soobshcheniya Akademii Nauk Gruzinskoy SSR. 100(1):197-200, 1980.

The effect of Nootropile on evoked transcallosal and primary response of the cerebral cortex was studied in unanesthetized curarized cats. Nootropile was administered intravenously (500mg/kg), or applied locally near the recording electrode (50% solution). Results show that Nootropile increased the amplitude of transcallosal responses, recorded from the somatosensory area of the cerebral cortex; Nootropile did not affect the primary responses of the same cortical area, elicited by stimulation of the contralateral forepaw. These results suggest that Nootropile has a specific effect on the cortical structures involved in the generation of transcallosal responses. 7 references. (Journal abstract modified)

003781 Edvinsson, Lars; Hardebo, Jan Erik; Lundh, Hakan. Dept. of Clinical Pharmacology, EA-blocket, University Hospital of Lund, S-221 85 Lund, Sweden **Action of 4-aminopyridine on the cerebral circulation.** Acta Neurologica Scandinavica. 63(2):122-130, 1981.

The vasomotor effects of 4-aminopyridine (4-AP), a compound which facilitates both inhibitory and excitatory synaptic activity in CNS, were examined in isolated feline brain vessels and in brain cortical metabolism and regional cerebral blood flow of rats. At high concentrations, a minor vasoconstriction was obtained of isolated pial vessels. Measurement of regional cerebral blood flow using the 14C-ethanol technique demonstrated significant increase in blood flow of caudate nucleus (93%), thalamus (74%), and cerebellum (82%). The arteriovenous oxygen difference of cortical tissue was reduced from 3.20mmol 02/ml to 1.69mmol 02/ml by 4-AP. This was not associated with an increase in cortical blood flow. Cortical metabolic rate of oxygen was unchanged by 4-AP. 24 references. (Author abstract modified)

003782 Einspahr, F. J.; Piercey, M. F. Piercey: CNS Research, Upjohn Company, Kalamazoo, MI 49001 **Morphine depresses dorsal horn neuron responses to controlled noxious and non-noxious cutaneous stimulation.** Journal of Pharmacology and Experimental Therapeutics. 213(3):456-461, 1980.

Morphine (0.3 to 3.0mg/kg i.v.) depressed the spontaneous activity, the electrically evoked discharge, and the response to noxious cutaneous heat of nociceptive dorsal horn neurons in unanesthetized, decerebrated, low spinal cats. In nociceptive neurons that received convergent nonnoxious inputs, morphine also depressed responses to nonnoxious cutaneous air puff stimulation. These morphine effects were reversed by 0.3mg/kg i.v. naloxone. In neurons that were purely nonnociceptive, morphine had little or no effect on spontaneous activity or on evoked responses to nonnoxious stimuli. 47 references. (Author abstract modified)

003783 El-Fakahany, Esam; Richelson, Elliott. Richelson: Dept. of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Involvement of calcium channels in short-term desensitization of muscarinic receptor-mediated cyclic GMP formation in mouse neuroblastoma cells.** Proceedings of the National Academy of Sciences of the United States. 77(11):6897-6901, 1980.

Evidence is presented that incubation of mouse neuroblastoma cells (clone N1E-115) with Mn2 results in a rapid and transient increase in cyclic GMP formation. This effect appears to be due to an increase in calcium influx because it does not occur in the absence of extracellular calcium or in the presence of verapamil, a calcium transport inhibitor. In addition, Mn2 inhibited muscarinic receptor mediated cyclic GMP responses. The ability of Mn2 to increase cyclic GMP levels was markedly diminished in cells desensitized to the effects of carbamoylcholine, suggesting that this desensitization involves inactivation of calcium entry. 33 references. (Author abstract modified)

003784 Eliasson, S. G.; Kiessling, L. A.; Scarpellini, JoAnne D. Dept. of Neurology, Washington University School of Medicine, St. Louis, MO 63110 **Ethanol-induced changes in cyclic guanosine 3',5'-phosphate metabolism in mouse vestibular region.** Neuropharmacology. 20(4):397-403, 1981.

Cyclic guanosine 3',5'-phosphate (GMP) content in the vestibular nuclei region of mouse brain increased after 10 to 14 days of ethanol intake. The increase was preceded by an increase in guanylate cyclase activity. A second increase in cyclic GMP level, accompanied by a decrease in cyclic GMP phosphodiesterase activity, was observed after 4 weeks on an ethanol containing diet. The initial increase in cyclic GMP was not as pronounced in DBA/2J mice as in C57BL/6J or AKR/J mice. Cerebellectomy had no effect on the ethanol-induced increases in cyclic GMP. 43 references. (Author abstract modified)

003785 Ennis, Christine; Cox, Barry. Dept. of Pharmacology, Materia, Medica and Therapeutics, Manchester University, Medical School, Manchester M13 9PT, England **The dopamine receptor antagonist domperidone is also a competitive antagonist at alpha1-adrenoceptors.** Journal of Pharmacy and Pharmacology. 32(6):434-435, 1980.

The potency of domperidone as an alpha1-adrenoceptor antagonist was tested in the guinea-pig aortic strip preparation. Against the alpha1-adrenoceptor agonist phenylephrine, domperidone was less potent than prazosin and spiroperidol, roughly equipotent to phentolamine, and more potent than haloperidol. Pimozide and metoclopramide were ineffective as antagonists of phenylephrine. Results show that domperidone possesses alpha1-adrenoceptor properties in addition to its reported dopamine receptor blocking activity. 7 references.

003786 Ennis, Christine; Cox, Barry. Bioscience II Dept., ICI Pharmaceuticals Ltd., Mereside, Alderley Park, Macclesfield, Cheshire, SK10 4TG, England **GABA enhancement of (3H)dopamine release from slices of rat striatum: dependence on slice size.** European Journal of Pharmacology. 70(3):417-420, 1981.

The effect of GABA on potassium evoked tritium release from slices of rat striatum preloaded with 3H-dopamine varied with slice size. GABA had no effect on the release of tritium from 100 x 100mcm ribbons of striatum, but produced a dose related enhancement of potassium evoked tritium released from 250 x 250mcm ribbons. The enhancement was antagonized by tetrodotoxin, but was not affected by bicuculline or picrotoxin. The effect of GABA was not mimicked by the GABA agonists muscimol and baclofen. Results suggest that an interneuron may be involved in the GABA effect, but antagonist studies indicated that the neurotransmitter released by the postulated interneuron was not acetylcholine, 5-hydroxytryptamine, glycine, glutamate, or enkephalin. 8 references. (Author abstract modified)

003787 Enns, Louise; McCoy, E. E. Dept. of Pediatrics, University of Alberta, Edmonton, Alberta, Canada **A study of gamma-aminobutyric acid uptake in normal and Down's syndrome platelets.** British Journal of Pharmacology. 71(2):553-556, 1980.

The initial rate of GABA uptake in platelets from Ss with Down's syndrome (DS) was reduced by 42%, compared to uptake in platelets from normal Ss. The rate of GABA uptake increased in both DS and normal platelets when the sodium ion concentration in the medium was increased. GABA uptake in the presence of 2,4-dinitrophenol or at 2 degrees C was approximately 56% of uptake at 37 degrees C in both DS and normal platelets. Extrapolation of a reciprocal plot revealed the presence of a two affinity uptake system. The deficit in GABA uptake in DS platelets suggests that decreased amine uptake and altered neurotransmission may exist in DS synaptosomes. 14 references. (Author abstract modified)

003788 Eroglu, L.; Hizal, A.; Koyuncuoglu, H. Dept. of Pharmacology and Clinical Pharmacology of Istanbul Medical Faculty, University of Istanbul, Capa, Istanbul, Turkey **The effect of long-term concurrent administration of chlorpromazine and lithium on the striatal and frontal cortical dopamine metabolism in rats.** Psychopharmacology. 73(1):84-86, 1981.

The effects of lithium and chlorpromazine chronically administered along and together on the dopamine metabolism in the rat striatum and frontal cortex was investigated by measurement of the levels of dopamine (DA) and its main metabolite, homvanillic acid (HVA). Long-term chlorpromazine administration caused a significant increase in the striatal DA level and a decrease in that of HVA and HVA/DA ratio without any changes in those of the frontal cortex. The prolonged administration of lithium elevated the striatal levels of both HVA and DA, but no change in the frontal cortex was observed. The concurrent administration of chlorpromazine and lithium caused a significant increase in the frontal cortical DA level and a decrease in that of HVA and HVA/DA ratio. The striatal DA and HVA levels increased under the effect of the combined treatment, while the HVA/DA ratio remained unchanged. 20 references. (Author abstract)

003789 Euvrard, Catherine; Oberlander, Claude; Boissier, Jacques R. Centre de Recherches Roussel UCLAF, F-93230 Romainville, France **Antidopaminergic effect of estrogens at the striatal level.** Journal of Pharmacology and Experimental Therapeutics. 214(1):179-185, 1980.

The increase in striatal acetylcholine (ACh) levels induced by apomorphine in Sprague-Dawley rats was blocked by moxestrol and other estrogens, but not by progestagens, androgens, or corticosteriods. The moxestrol effect increased with repeated treatment and lasted for at least 24 hours after the final injection. Moxestrol did not alter baseline striatal ACh levels, striatal choline acetyltransferase or acetylcholinesterase activities, or basal or apomorphine-induced decreases in striatal dopamine turnover. In rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal dopamine pathway, moxestrol antagonized the contralateral circling induced by apomorphine. The effect of moxestrol on the apomorphine-induced increase in striatal ACh was abolished by hypophysectomy and mimicked by pituitary transplants under the renal capsule. It is suggested that moxestrol exerts its antidopaminergic effect at the striatal level by decreasing dopaminergic postsynaptic transmission via mediation of the pituitary gland. 55 references. (Author abstract modified)

003790 Fang, Victor S. Endocrinology Laboratory, Dept. of Medicine, University of Chicago, Chicago, IL 60637 **Pharmacological difference of L-DOPA, apomorphine, and bromocriptine against metoclopramide.** Life Sciences. 28(19):2143-2149, 1981.

Male Sprague-Dawley rat serum prolactin was stimulated by metoclopramide and inhibited by L-DOPA, apomorphine, and bromocriptine. When injected 15 minutes after metoclopramide, bromocriptine was much less effective than L-DOPA and apomorphine in blocking the effect of metoclopramide on serum prolactin. When injected 15 minutes before metoclopramide, bromocriptine was the most effective antagonist of metoclopramide action. It is suggested that L-DOPA and apomorphine act exclusively by dopaminergic mechanisms, while bromocriptine and metoclopramide also act on the serotonergic pathways. 30 references. (Author abstract modified)

003791 Farsang, Csaba; Ramirez-Gonzalez, Maria Dolores; Mucci, Lucia; Kunos, George. Kunos: Dept. of Pharmacology and Therapeutics, McGill University, 3655 Drummond St., Montreal, Quebec, Canada H3G 1Y6 **Possible role of an endogenous opiate in the cardiovascular effects of central alpha adrenoceptor stimulation in spontaneously hypertensive rats.** Journal of Pharmacology and Experimental Therapeutics. 214(1):203-208, 1980.

In unanesthetized spontaneously hypertensive Okamoto-Aoki rats (SHR), naloxone (0.5 to 2mg/kg i.p.) and naltrexone (2mg/kg) inhibited the hypotension and bradycardia induced by clonidine (5 to 20mcg/kg i.v.). Naloxone also reversed the reduction in blood pressure and heartrate induced by chronic treatment of SHR with clonidine as well as the hypotension induced by a single injection of alpha-methyldopa. In pentobarbital anesthetized SHR, the hypotension and bradycardia induced by clonidine were inhibited by naloxone or yohimbine. Morphine also reduced blood pressure and heartrate in thse animals, these effects were antagonized by naloxone, but not by yohimbine. The reductions in blood pressure and heartrate by clonidine or alpha-methyldopa in normotensive Wistar-Kyoto rats were smaller than in SHR and were not influenced by naloxone. Results suggest that endogenous opioids are involved in the antihypertensive action of central alpha-adrenoceptor stimulants in SHR, but this mechanism appears to be absent or inactive in normotensive rats. 26 references. (Author abstract modified)

003792 Fekete, M. I. K.; Herman, J. P.; Kanyicska, B.; Pakovits, M. Institute of Experimental Medicine, Academy of Science, Budapest, Hungary **Dopamine, noradrenaline and 3,4-dihydroxyphenylacetic acid (DOPAC) levels of individual brain nuclei, effects of haloperidol and pargyline.** Journal of Neural Transmission. 45:207-218, 1979.

Noradrenaline (NA), dopamine (DA), and 3,4-dihydroxyphenylacetic acid (DOPAC) were determined with a newly developed radioenzymatic method simultaneously in the striatum, limbic system, hypothalamus, and catecholamine containing cell groups of the rat brain. Only a loose relationship was established between DOPAC and DA contents in the various brain areas. The lowest DOPAC/DA ratio was found in the median eminence, and the highest DOPAC/DA ratio was found in the periventricular nucleus of the hypothalamus. Haloperidol increased the DOPAC level in only the striatum, olfactory tubercle, and central amygdaloid nuclei, and decreased the DOPAC level in the locus coeruleus. Pargyline caused an approximate 50% decrease of DOPAC content of most of the nuclei in 10 minutes; the drug's effectiveness did not parallel that of haloperidol. The results are discussed as a consequence of different reactivity of various DAergic terminals and catecholamine cell bodies to haloperidol and pargyline. (Journal abstract modified)

003793 Freedman, Robert; Marwaha, Jwaharlal. Dept. of Psychiatry, C268, University of Colorado Health Sciences Center, 4200 E. Ninth Avenue, Denver, CO 80262 **Effects of acute and chronic amphetamine treatment on Purkinje neuron discharge in rat cerebellum.** Journal of Pharmacology and Experimental Therapeutics. 212(3):390-396, 1980.

The spontaneous discharge of the cerebellar Purkinje neuron in urethane anesthetized rats was investigated as an indicator of central noradrenergic activity during the acute and chronic administration of d-amphetamine. Acute parenteral administration of amphetamine caused a dose dependent slowing of the discharge. Since this effect is not seen in animals in which the catecholaminergic innervation has been selectively removed by previous treatment with 6-hydroxydopamine, it is hypothesized that the slowing is caused by the increased release and/or blocked reuptake of endogenous norepinephrine. Acute administration of amphetamine also increases the response of the Purkinje neurons to its afferent inputs: the excitatory climbing fibers and the inhibitory basket and stellate cells. These effects of amphetamine on spontaneous and evoked activity are similar to the effects of microiontophoretically applied norepinephrine. It is concluded that chronic amphetamine treatment may cause an increase in response to endogenous norepinephrine, both when spontaneously released and when released after acute amphetamine administration. 22 references. (Author abstract modified)

003794 Friedman, Eitan; Meller, Emanuel; Hallock, Marilyn. Dept. of Psychiatry, NYU Medical Center, New York, NY 10016 **Effects of conformationally restrained analogues of serotonin on its uptake and binding in rat brain.** Journal of Neurochemistry. 36(3):931-937, 1981.

Two series of serotonin (5-HT) analogues with the side chain amino acid group constrained in the gauche or trans conformation were used to study the preferred conformation of 5-HT for interaction with two different neuronal sites. Results showed that 6-hydroxytetrahydro-beta-carboline and 6-hydroxy-3-aminotetrahydrocarbazole are potent, competitive inhibitors of 5-HT uptake into male Sprague-Dawley rat hypothalamic synaptosomes. The 5-HT analogues were 20 to 30 times less potent in inhibiting synaptosomal transport of catecholamines and both showed poor affinity for the postsynaptic 5-HT receptor. These findings support the suggestion that 5-HT can assume at least three preferred conformations, with only small energy barriers to their interconversion. 27 references. (Author abstract modified)

003795 Fry, B. W.; Ciarlone, A. E. School of Dentistry, Medical College of Georgia, Augusta, GA 30912 **Effects of phenytoin on mouse cerebellar 5-hydroxytryptamine and norepinephrine.** Neuropharmacology. 20(6):623-625, 1981.

Norepinephrine and 5-hydroxytryptamine concentrations in male Swiss-Webster mouse cerebellum were determined after a single i.p. injection of phenytoin (20mg/kg). The 5-hydroxytryptamine concentrations were 98%, 122%, 104%, 105%, 112%, and 120% of control value at 2, 4, 10, 16, 22, and 28 hours after injection, respectively. At these times, the norepinephrine concentrations were 102%, 111%, 116%, 96%, 94%, and 120% of control value. Increases in these brain amines may be related to the anticonvulsant action of phenytoin. 10 references. (Author abstract modified)

003796 Fuller, Ray W.; Snoddy, Harold D.; Perry, Kenneth W. Lilly Research Lab., Eli Lilly and Co., Indianapolis, IN 46285 **Comparative effects of amantadine and amfonelic acid on dopamine metabolism in rat brain.** Brain Research Bulletin. 6(2):141-143, 1981.

The comparative effects of amantadine and amfonelic acid on dopamine (DA) metabolism in rat brain are described. Amantadine did not change basal levels of 3,4-dihydroxyphenylacetic acid (DOPAC) or homovanillic acid (HVA) in rat brain and did not alter the increase in DOPAC levels resulting from DA receptor blackade by spiperone. The increase in HVA levels produced by spiperone was significantly, but only slightly, enhanced by amantadine at these doses. In contrast, amfonelic acid at dose of 5mg/kg increased DOPAC and HVA levels and enhanced severalfold the spiperone-induced elevation of DIOAC and HVA levels. Amfonelic acid at a 2.5mg/kg dose enhanced the turnover of DA (measured by the decline in dopamine concentration after inhibition of tyrosine hydoxylation with alpha-methyltyrosine) in spiperone treated rats, whereas amantadine had a smaller and not significant effect. Neither compound affected DA levels in alpha-methyltyrosine treated rats not given spiperone. Although amantadine has been observed by other researchers to enhance the stimulation release of DA, it does not appear to act in a manner similar to amfonelic acid. 20 references. (Author abstract modified)

003797 Gale, Karen. Dept. of Pharmacology, Georgetown University Schools of Medicine and Dentistry, Washington, DC 20007 **Relationship between the presence of dopaminergic neurons and GABA receptors in substantia nigra: effects of lesions.** Brain Research. 210(1-2):401-406, 1981.

Submaximal destruction of nigrostriatal dopaminergic projections in male Sprague-Dawley rats produced a 25% decrease in specific GABA binding in the substantia nigra and reduced striatal tyrosine hydroxylase activity to 15 to 44% of control level. Lesions that caused maximal destruction of nigrostriatal dopamine neurons reduced striatal tyrosine hydroxylase to less than 15% of control, but did not alter specific GABA binding in the substantia nigra. Results suggest that two distinct processes occurred in response to destruction of dopamine neurons, the loss of GABA binding sites physically associated with nigral dopamine neurons and an increase in nigral GABA receptors associated with nondopaminergic neurons. The latter process may be due to a decrease in nigral GABA transmission secondary to the complete loss of dopaminergic synaptic activity in the striatum. 21 references. (Author abstract modified)

003798 Gallagher, Michela; Kapp, Bruce S.; McNall, Carol L.; Pascoe, Jeffery P. Dept. of Psychology, Davie Hall 013 A, University of North Carolina, Chapel Hill, NC 27514 **Opiate effects in the amygdala central nucleus on heart rate conditioning in rabbits.** Pharmacology Biochemistry and Behavior. 14(4)497-505, 1981.

Opiate agents were injected into the central nucleus of the amygdala complex of New Zealand white rabbits prior to classical conditioning or pseudoconditioning of heartrate responding. Opiate injection into the central nucleus did not significantly alter baseline heartrate, heartrate responding during habituation trials to presentations of the conditioned stimulus alone, or heartrate responding during the pseudoconditioning procedure. Opiate administration did alter the acquisition of a conditioned bradycardia response during classical conditioning trials in which the offset of the conditioned stimulus was coincident with the presentation of an aversive unconditioned stimulus.

The opiate agonist levorphanol (5.0nM) significantly impaired the acquisition of the conditioned bradycardia response; this stereospecific effect was blocked by concurrent administration of the opiate antagonist naloxone (2.5nM). Naloxone alone significantly increaseed the magnitude of the conditioned bradycardia response. The effects produced by opiate administration into the central nucleus were not observed after administration of the same agents into sites 1 to 2mm dorsal to the central nucleus. 37 references. (Author abstract modified)

003799 Garcia-Sevilla, J. A.; Magnusson, T.; Carlsson, A. Dept. of Pharmacology, University of Goteborg, Goteborg, Sweden **Opposite effects of naloxone on substance P-induced in brain dopa synthesis and in locomotor activity in rats.** Journal of Neural Transmission. 45:185-193, 1979.

The effects of substance-P and naloxone on the synthesis of dopamine and noradrenaline in rat brain and on rat behavior were studied. Intracerebroventricular injection of substance-P enhanced the synthesis of dopamine and noradrenaline, but these effects were blocked in most brain regions by pretreatment with naloxone. Substance-P also induced vasodilation, salivation, and increased locomotor activity, but these effects were not antagonized by naloxone and, in the case of locomotor activity, the effects were potentiated. The data suggest the existence of specific substance-P containing neuronal pathways for behavior, these pathways being unrelated to those regulating the synthesis of brain catecholamines. (Journal abstract modified)

003800 Gentleman, S.; Parenti, M.; Commissiong, J. W.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Dopamine-activated adenylate cyclase of spinal cord: supersensitivity following transection of the cord.** Brain Research. 210(1-2):271-275, 1981.

A dopamine activated adenylate cyclase was identified in a membrane fraction of male Sprague-Dawley rat spinal cord. The concentration of dopamine required to produce half maximal activation was about 5mcM; this activation was blocked by haloperidol. Apomorphine also activated the cyclase. Following transection of the cord, adenylate cyclase was about 5 to 10 times more sensitive to dopamine below the transection. Results indicate there are dopamine containing tracts in the spinal cord which could be involved in normal spinal mechanisms, in diseases associated with dopaminergic neurons, and in the side-effects of neuroleptic drugs. 10 references. (Author abstract modified)

003801 Giagnoni, G.; Santagostino, A.; Grassi, A.; Fumagalli, P.; Gori, E. Institute of Pharmacology, Faculty of Sciences, University of Milan, Via Vanvitelli 32/A, Milan, Italy **Role of adrenergic blocking agents and glucocorticoids on the regulation of pituitary opioid peptides levels.** Archives Internationales de Pharmacodynamie et de Therapie. 248(2):272-279, 1980.

Pituitary opioid peptide levels were determined in female Sprague-Dawley rats given single intracerebroventricular injections of alpha-methyl-p-tyrosine (AMPT, 4mg) or phentolamine (40mcg) and repeated subcutaneous injections of dexamethasone valerate (2.5mg/kg). Phentolamine produced an immediate rise in corticosteroid levels and an increase in pituitary endorphin content after 20 minutes. AMPT increased serum corticosterone and reduced hypothalamic norepinephrine concentration, but did not affect pituitary endorphin levels. Repeated steroid treatment decreased serum corticosterone levels and pituitary opioid activity (primarily due to a reduction of beta-endorphin content). It is suggested that the pituitary endorphin system, like ACTH, is under negative direct or indirect regulatory control of glucocorticoids. 17 references. (Author abstract modified)

003802 Gillan, Maureen G. C.; Kosterlitz, H. W.; Paterson, S. J. Unit for Research on Addictive Drugs, University of Aberdeen, Aberdeen, Scotland **Comparison of the binding characteristics of tritiated opiates and opioid peptides.** British Journal of Pharmacology. 70(3):481-490, 1980.

The dissociation equilibrium constants and the maximal number of binding sites for various tritiated ligands of opiate receptors were studied in homogenates of guinea-pig brain. Inhibitory constants for unlabeled ligands against tritiated ligands were also determined. Results revealed different binding capacities for the different tritiated ligands. Data supported the hypothesis that naturally occurring opioid peptides (met-enkephalin, leu-enkephalin, and beta-endorphin) can interact with at least two receptors, the mu-receptor and the delta-receptor. 26 references. (Author abstract modified)

003803 Giusti, G. V.; Chiarotti, M.; Vigevani, F. Ist. Med. Leg., Universita di Cattania, Roma, Italy **Neutralization of the effect of delta9-tetrahydrocannabinol on barbiturate sleeping time by specific active immunization.** Drug and Alcohol Dependence. 5:185-187, 1980.

Adult mice were actively immunized with delta9-tetrahydrocannabinol bovine serum albumin (delta9-THC-BSA) conjugate. Control animals were immunized with BSA alone. While the administration of phentobarbital and delta9-THC to control animals resulted in the well known prolongation of the barbiturate sleeping time, in mice immunized with delta9-THC-BSA conjugate this effect was almost completely neutralized. (Journal abstract)

003804 Gogolak, G.; Stumpf, Ch. Dept. of Neuropharmacology, Brain Research Institute, Austrian Academy of Sciences, A-1090 Vienna, Wahringerstrasse 13a, Austria **Action of drugs on the cerebellar electrical activities.** Progress in Pharmacology. 3(2):1-66, 1980.

Spontaneous and drug-induced cerebellar electrical activities recorded from in situ preparations, cerebellar slices, and tissue cultures are reviewed. The effects of central depressants such as barbiturates and benzodiazepines and of convulsants, anticonvulsants, and related agents (benzylpenicillin, pentetrazol, strychnine, harmaline, local anesthetics, and phenytoin) are discussed. Actions of putative neurotransmitters, cholinergic and anticholinergic agents, adrenergic and adrenolytic agents, and amino acids are also considered. 281 references.

003805 Goltermann, N. R.; Stengaard-Pedersen, K.; Rehfeld, J. F.; Christensen, N. J. Institute of Medical Biochemistry, University of Aarhus, DK-8000 Aarhus C, Denmark **Newly synthesized cholecystokinin in subcellular fractions of the rat brain.** Journal of Neurochemistry. 36(3):959-965, 1981.

The subcellular localization of newly synthesized cholecystokinin (CCK) in various parts of Wistar rat brain was studied after intracisternal pulse injections of (35S)methionine. De novo synthesized CCK in the crude mitochondrial/synaptosomal fraction and in the purified synaptosomal fraction was demonstrated by affinity chromatography, using antibodies specific for the COOH terminal sequence of CCK. Subsequent gel chromatography revealed two molecular forms of labeled CCK with elution constants of 1.1 (corresponding to the COOH terminal tetrapeptide amide, CCK-4) Results support the suggestion that the small molecular forms are transmitter forms of CCK. 16 references. (Author abstract modified)

003806 Gospe, Sidney M., Jr.; Wilson, Wilkie A., Jr. Wilson: Epilepsy Center Research Laboratory, Bldg. 2, V.A. Medical Center, Durham, NC 27705 **Dopamine inhibits burst-firing of**

neurosecretory cell R 15 in Aplysia californica: establishment of a dose-response relationship. Journal of Pharmacology and Experimental Therapeutics. 214(1):112-118, 1980.

Burst firing in neurosecretory cell R-15 of Aplysia californica was inhibited by the bath application of dopamine. Dopamine reduced the inward current in the region of negative slope conductance and tended to linearize the current/voltage curve. The loss of inward current in the region of negative slope conductance was dose dependent, highly reproducible, and relatively resistant to desensitization. The dose/response curve was sigmoidal in shape, rising from minimal effect near 50mcM to a maximal effect near 500mcM. This dose/response curve can be used as a standard of comparison in studies of agonists and antagonists. 24 references. (Author abstract modified)

003807 Goto, Masayoshi; Inomata, Norio; Ono, Hideki; Saito, Ken-Ichi; Fukuda, Hideomi. Dept. of Toxicology and Pharmacology, Faculty of Pharmaceutical Sciences, University of Tokyo, Bunkyo-ku, Tokyo 113, Japan **Changes of electroretinogram and neurochemical aspects of GABAergic neurons of retina after intraocular injection of kainic acid in rats.** Brain Research. 211(2):305-314, 1981.

The effects of intraocular injections of kainic acid (KA) on electroretinogram (ERG) readings and neurochemical properties of the retina were examined in male Wistar rats. Histological alterations were evident 1 hour after injection: swelling was observed in the inner and outer plexiform layers, and certain ganglion cells and cells of the inner nuclear layers exhibited pyknotic nuclei. Most of the ganglion cells appeared to have degenerated within 48 hours, and the form of the outer plexiform layer was incomplete. The amplitude of the b-waves of the ERG decreased 2 hours after injection and never recovered, whereas the amplitude of the a-waves was unaffected by a 50nmol dose of KA and increased by a 200nmol dose. GABA content in the eyecups began to decrease within 1 hour and fell to 20% of its original level within 24 hours. Glutamic acid decarboxylase activity was unaffected 2 hours after injection but was reduced to 40% of its original level within 24 hours. Taurine was not altered by KA. 31 references. (Author abstract modified)

003808 Govoni, S.; Hong, J. S.; Yang, H.- Y. T.; Costa, E. Yang: Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Increase of neurotensin content elicited by neuroleptics in nucleus accumbens.** Journal of Pharmacology and Experimental Therapeutics. 215(2):413-417, 1980.

Increases of neurotensin content of nucleus accumbens elicited by neuroleptics were investigated. Neurotensin immunoreactive material (neurotensin IR) of nucleus accumbens increased 16 hours after a single injection of haloperidol; this increase persisted for 8 hours or longer. Repeated injections of haloperidol caused a gradual and progressive increase of neurotensin IR. Maximal responses were obtained with 1mg/kg/day in 3 weeks. The increase of neurotensin IR material of nucleus accumbens was elicited also by chlorpromazine, trifluoroperazine and pimozide, while promazine and promethazine were ineffective. These data suggest a neuroleptic modulation of neurotensin metabolism, synthesis, or utilization directly or indirectly through dopaminergic synapses. 34 references. (Author abstract modified)

003809 Grandison, L.; Guidotti, A. Dept. of Physiology and Biophysics, Rutgers Medical School, Piscataway, NY **Role of the anterior pituitary GABA receptor in the control of prolactin release.** In: Brambilla, F., ed., Progress in psychoneuroendocrinology. New York, Elsevier/North Holland, 1980. 669 p. (p. 157-163).

Evidence is presented to support the hypothesis that GABA receptors in the anterior pituitary regulate release of prolactin (PRL). GABA receptors have been identified in membrane preparations of rat and human pituitary. Incubation of hemisected anterior pituitaries with the GABA agonist muscimol inhibits PRL release. The high concentration of GABA in human pituitary suggests that the pituitary is a target for GABA released under physiological conditions, even though the pituitary is not the source of GABA. The most likely source is the tuberoinfundibular GABA neuron, which may secrete GABA into the portal pituitary circulation. Unlike the tuberoinfundibular dopamine neuron, the GABA neuron does not appear to have a role in maintaining basal PRL release. 26 references.

003810 Grant, Steven J.; Redmond, D. E., Jr. Dept. of Psychiatry, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **The neuroanatomy and pharmacology of the nucleus locus coeruleus. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-31176, 1980. 49 p.

Research is reviewed on the neurophysiological and neuropharmacological characteristics of the nucleus locus coeruleus (LC) in the rat, a brain region which contains specialized catecholamine containing cells. Emphasis is on how the interaction of clonidine with noradrenergic nuclei, such as LC, might be responsible for clonidine's psychopharmacological properties. These results indicate that: 1) clonidine acts preferentially at alpha-2-adrenergic receptors, and in systemic doses of less than 50 to 100mcg/kg, clonidine exerts its effects at autoreceptors which initially decrease noradrenergic neuronal firing rates, norepinephrine (NE) release, and NE turnover; 2) this action produces functional decreases of the usual effects of these neurons at their postsynaptic alpha-1-adrenergic and beta-adrenergic receptor mediated projections; and 3) higher doses of clonidine produce agonist effects at alpha-1-adrenergic receptors, counteracting the effects of decreases in firing rate and turnover, while decreased function continues at beta-receptors. It is concluded that receptors for GABA, endorphins, substance-P, and acetylcholine on LC neurons provide an anatomical and physiological basis for interactions among systems using these substances as neurotransmitters by acting on a final noradrenergic common pathway. The noradrenergic pathways, in turn, also project and alter function in areas utilizing other neurotransmitters, and studies of LC may help determine the nature and effects of clonidine and other alpha-2-agonists on the brain. 107 references.

003811 Greeley, George H., Jr.; Kizer, J. S. Room 241, Biological Sciences Research Center (220H), University of North Carolina School of Medicine, Chapel Hill, NC 27514 **The effects of chronic methylphenidate treatment on growth and endocrine function in the developing rat.** Journal of Pharmacology and Experimental Therapeutics. 215(3):545-551, 1980.

The effects of chronic methylphenidate treatment on growth and endocrine function in the developing rat were investigated. At 35mg/kg per day and 100mg/kg per day, methylphenidate significantly decreased rate of skeletal growth and bodyweight gain in both males and females. Vaginal patency in females given 35mg/kg and 100mg/kg during neonatal life was significantly delayed and number of estrous cycles after cessation of chronic treatment was significantly reduced. In both males and females, chronic methylphenidate depresses serum prolactin levels at all doses, an effect which disappears after cessation of treatment. At all doses, chronic methylphenidate significantly decreases basal serum insulin levels. Chronic methylphenidate treatment significantly depresses growth hormone levels in females, with no consistent effect in males. In females, chronic methylphenidate has no consistent effect upon gonadotropin levels but significantly decreases luteinizing hormone and follicle stimulating hormone levels in males. 12 references. (Author abstract modified)

003812 Green, Kenneth F. California State University, 6101 East 7th St., Long Beach, CA 90801 **Hippocampal slow activity: two input systems? (Unpublished paper).** Final Report, NIMH Grant R03-MH-32873, 1980. 7 p.

Inputs to the hippocampal formation that may affect an electrical rhythmic slow activity (RSA) in rats were investigated. Data obtained from 30 Ss indicated that with urethane, the RSA amplitude profile replicated profile past findings, as did RSA frequencies of 3 to 7 Hz. Atropine reduced percent time RSA while eserine increased percent time RSA. Stimulation of the performant path (PP) at RSA frequencies did not drive RSA in any reliable fashion. Stimulation of medial septal area (MS) at 50 to 60 Hz elicited RSA and, to a limited extent, increased RSA frequency as MS stimulation intensity increased. The findings indicated that RSA is not affected reliably by electrical stimulation of PP in urethane anesthetized rats. The results also suggest that the entorhinal cortex is not a driver of RSA in the hippocampus, even under the conditions which favor its appearance (urethane anesthesia, attention related input, slow stimulation rates, and eserine). If this result holds up in waking rats, several problems are seen to exist. It is recommended that fine analysis of cellular mechanisms should be reconciled with field potentials in future research.

003813 Grignolo, Alberto; Light, Kathleen C.; Obrist, Paul A. Dept. of Pharmacology, P.O. Box 3813, Duke University Medical Center, Durham, NC 27710 **Beta-adrenergic influence on cardiac dynamics during shock-avoidance in dogs.** Pharmacology Biochemistry and Behavior. 14(3):313-319, 1981.

The role of beta-adrenergic receptors in the mediation of the cardiodynamic effects of a shock avoidance task were evaluated in conscious dogs. Shock avoidance evoked reliable increases in left ventricular pressure (LV dP/dt), heartrate (HR), cardiac output (CO), systolic blood pressure (SBP), and diastolic blood pressure (DBP), as well as decreases in total peripheral resistance. Beta-adrenergic blockade by practolol (2 to 4mg/kg) eliminated the LV dP/dt increases, attenuated vasodilation and increases in HR and CO, diminished SBP increases in certain animals, and had no effect on DBP increases. Stable interindividual differences in the magnitude of LV dP/dt and HR increases during shock avoidance were demonstrated, but these differences were abolished by beta blockade. 32 references. (Author abstract modified)

003814 Gripenberg, J.; Heinonen, E.; Jansson, S. -E. Heinonen: Dept. of Physiology, University of Helsinki, Siltavuorenpenger, SF-00170 Helsinki 17, Finland **Uptake of radiocalcium by nerve endings isolated from rat brain: kinetic studies.** British Journal of Pharmacology. 71(1):265-271, 1980.

The uptake of radiocalcium by nerve ending particles isolated from male Sprague-Dawley rat brain was studied in vitro by means of a rapid lanthanum quenching technique. During control conditions and during high potassium stimulation, the uptake fit a theoretical three compartment model with two separate uptake phases, a fast initial phase followed by a late slow phase. The uptake as a function of external calcium concentration could be described in terms of Michaelis-Menten kinetics during high potassium stimulation; the fit was not as good under control conditions. The affinity for uptake of calcium remained unchanged during control conditions, but decreased drastically during the late slow phase of uptake under high potassium conditions. For both fast and slow phases of uptake, the maximal velocity of calcium uptake during high potassium stimulation was twice that observed under control conditions. Magnesium ion had an inhibitory effect on uptake, particularly during high potassium stimulation. Tetrodotoxin had a slight inhibitory effect additional to that exerted by magnesium ion during the initial phase of uptake into potassium stimulated synaptosomes. 21 references. (Author abstract modified)

003815 Gripenberg, J.; Heinonen, E.; Jansson, S. -E. Heinonen: Dept. of Physiology, University of Helsinki, Siltavuorenpenger, SF-00170 Helsinki 17, Finland **Uptake of radiocalcium by nerve endings isolated from rat brain: pharmacological studies.** British Journal of Pharmacology. 71(1):273-278, 1980.

The uptake of radiocalcium by nerve ending particles isolated from male Sprague-Dawley rat striatum was studied, using lanthanum as a quenching agent. High-potassium-induced calcium uptake occurred in two phases, an initial rapid phase and a late slow phase. Following preincubation with calcium chloride, dopamine reduced high-potassium-induced calcium uptake during the initial rapid phase, but had no effect on the late slow uptake phase. Haloperidol had no direct effect on calcium uptake, but abolished the inhibitory effect of dopamine on the initial rapid phase of high-potassium-induced uptake. Dibutyryl cyclic AMP and prostaglandin-E1 had no effect on the initial rapid phase of high-potassium-induced calcium uptake by striatal synaptosomes. Results suggest that dopamine regulates the depolarization-induced influx of calcium in presynaptic nerve endings in the striatum. 27 references. (Author abstract modified)

003816 Gross, Gerhard; Brodde, Otto-Erich; Schumann, Hans-Joachim. Pharmakologisches Institut der Universitat Essen, Hufelandstrasse 55, D-4300 Essen, West Germany **Regulation of alpha1-adrenoceptors in the cerebral cortex of the rat by thyroid hormones.** Naunyn-Schmiedeberg's Archives of Pharmacology. 316(1);45-50, 1981.

The influence of thyroid hormones on alpha1-adrenoceptors in a crude membrane fraction from male Wistar rat cerebral cortex was studied using the 3H-WB-4101 binding assay. The maximal number of 3H-WB-4101 binding sites was increased by 27% in cortical membranes from animals made hyperthyroid by 6-propyl-2-thiouracil feeding for 8 weeks and was reduced by 23% in animals made hypothyroid by 9 days of triiodothyronine injections. Triiodothyronine treatment reversed the reduction in 3H-WB-4101 binding induced by 6-propyl-2-thiouracil. No change in receptor affinity was observed. Inhibition of 3H-WB-4101 binding by adrenergic agonists and antagonists revealed no differences between euthyoroid and hypothyroid animals. It is concluded that thyroid hormones regulate the number of alpha1-adrenoceptors in membranes of rat cerebral cortex. 36 references. (Author abstract modified)

003817 Gross, P. M.; Teasdale, G. M.; Angerson, W. J.; Harper, A. M. Teasdale: Dept. of Neurosurgery, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland **H2-receptors mediate increases in permeability of the blood-brain barrier during arterial histamine infusion.** Brain Research. 210(1-2):396-400, 1981.

Infusion of histamine into the internal carotid artery of Sprague-Dawley rats increased cerebrovascular permeability to isotopically labeled sucrose. Prior administration of the histamine H2-receptor antagonist metiamide attenuated or blocked this response. It is concluded that intravascular histamine stimulates H2-receptors of cerebral endothelia and increases permeability of the blood-brain barrier. 28 references.

003818 Guchhait, Ras B. Johns Hopkins University, Charles & 34th Streets, Baltimore, MD 21218 **Regulation of biogenesis of**

psychotomimetic amines. (Unpublished paper). Final Report, NIMH Grant 5R01-MH-27256. 1980. 9p.

The roles of S-adenosylmethionine (SAM) and of 5-methyl-tetrahydrofolate (MTHF) as physiological methyl group donors for biogenic amine transmethylation were studied. Rat brain and pineal tissues were used as the enzyme sources. It was established that MTHF is not a methyl donor for methylation of biogenic amines. The results indicate that the pineal gland generates its own SAM, the only physiological methyl donor for biogenic amines. The major product of pineal MAT was identified as S-adenosyl-L-methionine by three techniques. The results indicate that the pineal organ from rat and various other species is enriched with MAT enzyme. The MAT enzyme is also present in rat Harderian gland and retina.

003819 Gundersen, Cameron B.; Jenden, Donald J. Dept. of Pharmacology, School of Medicine, University of California, Los Angeles, CA 90024 **Oxotremorine does not enhance acetylcholine release from rat diaphragm preparations.** British Journal of Pharmacology. 70(1):8-10, 1980.

Oxotremorine (10mcM) caused no significant change in the spontaneous or evoked release of acetylcholine (ACh) from the rat phrenic nerve/diaphragm preparation. No significant change in tissue levels of ACh or choline was observed with 10mcM oxotremorine, although a small reduction in tissue ACh was observed with 100mcM oxotremorine. The findings are not consistent with the dramatic oxotremorine-induced increase in ACh previously reported in this preparation. 11 references. (Author abstract modified)

003820 Gundersen, Cameron B.; Jenden, Donald J. Jenden: Dept. of Pharmacology, School of Medicine, University of California, Los Angeles, CA 90024 **Alterations of acetylcholine and choline metabolism in mammalian preparations treated with beta-bungarotoxin.** Journal of Neurochemistry. 36(3):938-948, 1981.

A gas chromatographic/mass spectrometric assay was used to study the effects of beta-bungarotoxin on acetylcholine (ACh) and choline (Ch) metabolism in central and peripheral cholinergic preparations. Beta-bungarotoxin did not inhibit the high affinity uptake of labeled Ch or the synthesis of ACh in male Sprague-Dawley rat brain synaptosomal fractions. However, when incubated with synaptosomal fractions, the toxin significantly increased the amount of Ch in the medium. Beta-bungarotoxin also caused a large increase in ACh release from rat brain minces and a depletion of the ACh content of minces. A similar phenomenon was observed in diaphragm preparations exposed continuously to beta-bungarotoxin, but an increase in ACh content was seen in diaphragms treated with the toxin for only 30 minutes. Beta-bungarotoxin had no measurable effect on ACh turnover in smooth muscle preparations from guinea-pig ileum. 30 references. (Author abstract modified)

003821 Gunion, Mark W.; Brown, Danley F.; Peters, Ronald H.; Novin, Donald. Peters: Dept. of Psychology, Iowa State University, Ames, IA 50011 **Unimpaired quinine metabolism in rats with ventromedial hypothalamic lesions.** Pharmacology Biochemistry and Behavior. 14(3):283-286, 1981.

In vitro rates of quinine metabolism were studied in female Long-Evans hooded rats with lesions of the ventromedial hypothalamus (VMH). Determinations were made under basal conditions and under conditions known to cause induction of drug metabolizing enzymes. The rate of drug metabolism in VMH lesioned rats was nearly identical to that in controls under all conditions tested. Results indicate that impaired quinine metabolism cannot account for the heightened sensitivity of VMH lesioned animals to the food intake suppressing effect of dietary quinine. 24 references. (Author abstract modified)

003822 Gyorgy, L.; Doda, M. Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest 1450, POB 67, Hungary **Influence of the dopaminergic agonists bromocriptine, piribedil and nomifensine on the sympathetic neural transmission in the nictitating membrane of the cat.** Archives Internationales de Pharmacodynamie et de Therapie. 249(1):4-11, 1981.

The effects of dopaminergic drugs on nictitating membrane contractions induced by cervical sympathetic nerve stimulation were studied in cats. Bromocriptine and piribedil injected into the lingual artery inhibited contractions induced by nerve stimulation, but did not suppress the effect of noradrenaline. In animals pretreated with desipramine, high doses of nomifensine inhibited contractions induced by nerve stimulation or by noradrenaline. Haloperidol and sulpiride both antagonized the inhibitory effect of piribedil, and sulpiride prevented the effect of bromocriptine. Results suggest that these agonists have a specific inhibitory effect on presynaptic dopaminergic receptors. 16 references. (Author abstract modified)

003823 Haga, Tatsuya; Haga, Kazuko. Dept. of Biochemistry, Hamamatsu University School of Medicine, Handa-cho, Hamamatsu 431-31, Japan **Characterization by (3H)dihydroergocryptine binding of alpha-adrenergic receptors in neuroblastoma x glioma hybrid cells.** Journal of Neurochemistry. 36(3):1152-1159, 1981.

The binding of tritiated dihydroergocryptine (3H-DHE) to sites in membranes from neuroblastoma/glioma hybrid cells (NG-108-15) with characteristics of alpha-adrenergic receptors was demonstrated. The binding was saturable and of high affinity. The specificity of the binding site for various ligands was more similar to that of alpha2-receptors than that of alpha1-receptors. Guanosine triphosphate lowered the affinity of agonists for the 3H-DHE binding site, but the nucleotide did not markedly affect the affinity of antagonists. 31 references. (Author abstract modified)

003824 Hall, Hakan; Ogren, Sven-Ove. Dept. of Pharmacology, Research and Development Laboratories, Astra Lakemedel AB, S-151 85, Sodertalje, Sweden **Effects of antidepressant drugs on different receptors in the brain.** European Journal of Pharmacology. 70(3):393-407, 1981.

Radioligand receptor binding techniques were used to characterize the effects of different structural types of antidepressant drugs on neurotransmitter receptors. Tricyclic antidepressants were relatively potent inhibitors of 3H-mepyramine, 3H-d-lysergic acid diethylamide (d-LSD), 3H-quinuclidinyl benzilate (QNB), and 3H-WB4101 binding to male Sprague-Dawley rat brain preparations. The potency of nontricyclic antidepressants varied greatly. Mianserin potently displaced 3H-mepyramine, 3H-d-LSD, and 3H-WB4101, but was a very weak displacer of 3H-QNB binding. Nomifensine, zimelidine, and alaproclate had very low affinity for these receptors. None of the antidepressants studied were active against the binding of 3H-dihydroalprenolol, 3H-spiroperidol, 3H-flunitrazepam, 3H-muscimol, and 3H-naloxone. Results are discussed in relation to biogenic amine theories of affective disorders. 76 references. (Author abstract modified)

003825 Hamon, M.; Mallat, M.; Herbet, A.; Nelson, D. L.; Audinot, M.; Pichat, L.; Glowinski, J. Groupe NB, INSERM U114, College de France, 11 place Marcelin Berthelot, F-75231 Paris Cedex 05, France **(3H)Metergoline: a new ligand of serotonin receptors in the rat brain.** Journal of Neurochemistry. 36(2):613-626, 1981.

A specific, high affinity binding site for 3H-metergoline was found in microsomal and synaptic plasma membranes from various areas of adult male rat brain. Experiments with 5,7-dihydroxytryptamine and kainic acid lesions indicated that this specific binding site was located postsynaptically with respect to serotonergic neurons. Serotonin was 400 times more potent than dopamine and noradrenaline in displacing bound 3H-metergoline in the hippocampus, but only 10 times more potent than dopamine in the striatum. Results suggest that 3H-metergoline binds to serotonin receptors in the hippocampus and to serotonin and possibly dopamine receptors in the striatum. 36 references. (Author abstract modified)

003826 Hanson, G.; Alphs, L.; Pradhan, Sikta; Lovenberg, W. Lovenberg: Section on Biochemical Pharmacology, NHBLI, NIH, Bethesda, MD 20205 **Response of striatonigral substance P systems to a dopamine receptor agonist and antagonist.** Neuropharmacology. 20(6):541-548, 1981.

Alterations in dopamine (DA) receptor activity significantly altered levels of substance-P-like immunoreactivity (SPI) in the susbtantia nigra of male Sprague-Dawley rats. DA receptor activation by apomorphine and receptor blockade by haloperidol both induced specific, dose dependent, and reversible decreases in the concentration of nigral SPI. Pretreatment with haloperidol antagonized the effect of apomorphine. Results suggest that DA receptor activity, mediated by the nigrostriatal DA system, exerts significant influence on the substance-P striato-nigral feedback loop. 41 references. (Author abstract modified)

003827 Harris, R. Adron; Hood, William F. Dept. of Pharmacology, University of Missouri School of Medicine, Columbia, MO 65212 **Inhibition of synaptosomal calcium uptake by ethanol.** Journal of Pharmacology and Experimental Therapeutics. 213(3):562-568, 1980.

In vitro addition of ethanol or pentobarbital to synaptosomes isolated from male Sprague-Dawley rat or Swiss-Webster mouse brain inhibited the depolarization dependent uptake of calcium, but did not affect uptake under nondepolarizing conditions. Synaptosomes from mice chronically ingesting ethanol were tolerant to the inhibitory effects of ethanol and pentobarbital, but not to the inhibitory effects of acetaldehyde. Synaptosomes from ethanol tolerant/dependent mice accumulated less calcium in the absence of ethanol than did synaptosomes from control mice. This depression of uptake was reversed by in vitro exposure of the synaptosomes to a low concentration of ethanol, suggesting it represents a biochemical response to the withdrawal of ethanol. A single injection of ethanol 1 hour before sacrifice did not alter the calcium uptake activity or drug sensitivity of the synaptosomes. Results suggest that the known inhibitory effects of ethanol and pentobarbital on the stimulated release of neurotransmitters and the development of tolerance to these effects may be mediated by the inhibition of the depolarization dependent influx of calcium by these drugs. 38 references. (Author abstract modified)

003828 Haubrich, D. R.; Gerber, N.; Pflueger, A. B.; Zweig, M. Merck Institute for Therapeutic Research, West Point, PA 19486 **Tissue choline studied using a simple chemical assay.** Journal of Neurochemistry. 36(4):1409-1417, 1981.

An enzymatic/radioisotopic assay was used to measure free choline in unextracted tissue in humans and animals. The lowest concentration of free choline in any tissue studied was present in human cerebrospinal fluid. A postmortem increase in concentration of free choline occurred in the blood, kidney, and liver of mice. Several treatments were found to increase the concentration of free choline. For example, intraperitoneal administration of choline or 2-amino-2-methyl-propanol (a choline oxidase inhibitor) induced an increase in the level of choline in blood, kidneys, liver, and brain of mice, and administration of 2-dimethylaminoethanol (deanol) caused an increase in kidney and liver choline. The level of choline in blood was increased when rats were treated orally with either antibiotics or esters of choline such as phosphorylcholine, glycerylphosphorylcholine, laroylcholine, or propionylcholine. Results show that the concentration of free choline may be regulated by intestinal metabolism, availability of esterified precursors, and activity of enzymes that metabolize choline. 43 references. (Author abstract modified)

003829 Haycock, Dean A.; Patrick, Robert L. Patrick: Box G., Brown University, Providence, RI 02912 **Catecholamine synthesis regulation in hypothalamic synaptosomes. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-31706, 1980. 34 p.

To characterize the properties of synaptosomal catecholamine formation in a predominantly noradrenergic preparation, catecholamine synthesis in rat brain hypothalamic synaptosomes was studied. Kinetic analysis revealed an apparent km for tyrosine of 2.5 micrometers and an apparent Vmax of 2.1 nmol/h/g. In the hypothalamus, norepinephrine-induced synthesis inhibition was reversed completely by preincubation with desipramine, a blocker of catecholamine uptake into noradrenergic tissue. Desipramine was relatively ineffective in the predominantly dopaminergic striatum, indicating that most of the catecholamine synthesis observed in the hypothalamic synaptosomes was taking place in noradrenergic, as opposed to dopaminergic, terminals. Synthesis was stimulated about 30% in the hypothalamus by elevated potassium, and this was antagonized markedly in a calcium free buffer and by the addition of tetraethylammonium chloride. Phenylethylamine compounds produced either stimulation (amphetamine) or inhibition (tyramine). The most effective synthesis stimulator was dibutyryl cyclic AMP. Lowering the pH of the incubation buffer increased the basal rate but decreased the stimulatory response to elevated potassium. These data suggest that synaptosomal preparations for the hypothalamus are useful in studying drug effects on catecholamine synthesis in noradrenergic terminals. 24 references. (Author abstract modified)

003830 Hays, Sally E.; Poland, Russell E.; Rubin, Robert T. Rubin: Division of Biological Psychiatry, Dept. of Psychiatry, Harbor-CLA Medical Center, Torrance, CA 90509 **Prolactin releasing potencies of antipsychotic and related nonantipsychotic compounds in female rats: relation to clinical potencies.** Journal of Pharmacology and and Experimental Therapeutics. 214(2):362-367, 1980.

The relationship between the clinical potency and ability to release prolactin in female rats was investigated in various antipsychotic and related nonantipsychotic drugs. Prolactin response to various intraperitoneal doses of nine antipsychotic and related nonantipsychotic compounds indicate that at doses of 50mg/kg or less, all drugs stimulated prolactin release into sera. The rank order of prolactin stimulation did not agree entirely with the ranking of relative antipsychotic potency of the compounds. The relations between prolactin stimulating potency and reported clinical potency was improved by comparing drugs within the same chemical classification. Reduced haloperidol, a major metabolite of haloperidol, was one fourth as potent as haloperidol in stimulating prolactin release, suggesting that the potential antipsychotic activity of reduced haloperidol should be investigated. 36 references. (Author abstract modified)

003831 Heikkila, John J.; Brown, Ian R. Brown: Dept. of Zoology, Scarborough College, University of Toronto, West Hill, Ontario M1C 1A4, Canada **Comparison of the effect of intravenous administration of d-lysergic acid diethylamide on free and membrane-bound polysomes in the rabbit brain.** Journal of Neurochemistry. 36(3):1219-1228, 1981.

Intravenous administration of d-lysergic acid diethylamide (LSD) to male New Zealand white rabbits resulted in disaggregation of free and membrane bound polysomes. Free polysomes were more sensitive than membrane bound polysomes to the drug. The degree of brain polysome shift was correlated with the extent of LSD-induced hyperthermia, and disaggregation was not observed when LSD-induced hyperthermia was prevented by maintaining the animals at 4 degrees. Induction of hyperthermia by elevation of ambient temperature also resulted in a shift in free and membrane bound polysomes. The disaggregation of polysomes to monosomes was not caused by ribonuclease activation. During polysome disaggregation, polyadenylated messenger RNA associated with free and membrane bound polysomes was relocalized from polysomes to monosomes. 57 references. (Author abstract modified)

003832 Heikkila, John J.; Cosgrove, James W.; Brown, Ian R. Brown: Dept. of Zoology, Scarborough College, University of Toronto, West Hill, Ontario, M1C 1A4, Canada **Cell-free translation of free and membrane-bound polysomes and polyadenylated mRNA from rabbit brain following administration of d-lysergic acid diethylamide in vivo.** Journal of Neurochemistry. 36(3):1229-1238, 1981.

Free and membrane bound polysomes and polyadenylated messenger RNA (mRNA) isolated from male New Zealand rabbit brain were translated in an mRNA dependent rabbit reticulocyte lysate system. Electrophoretic analysis of the cell free translation products indicate that most of the nascent proteins were common to free and membrane bound polysomes, but some qualitative and quantitative differences were observed. Compared with results obtained with purified polyadenylated mRNA, the addition of intact polysomes to the cell free translation assay was more efficient and produced higher molecular weight products. After hyperthermia induced by elevated ambient temperature products of free and membrane bound polysomes included a new 74K protein. 36 references. (Author abstract modified)

003833 Herkenham, Miles. Laboratory of Neurophysiology, NIMH, Bethesda, MD 20205 **Anesthetics and the habenulo-interpeduncular system: selective sparing of metabolic activity.** Brain Research. 210(1-2):461-466, 1981.

Regional localization of brain metabolism by (14C)deoxyglucose during anesthesia in male Sprague-Dawley rats showed that pentobarbital, ether, and chloral hydrate reduced deoxyglucose uptake in most neuronal regions. However, metabolism was unaltered or increased in the medial habenula, interpeduncular nucleus, and habenulointerpeduncular tract. Prior destruction of afferent inputs abolished the selective metabolic sparing in the habenulointerpeduncular system during chloral hydrate anesthesia. 13 references. (Author abstract modified)

003834 Hermann, A. University of Konstanz, Fakultat fur Biologie, D-7750 Konstanz, West Germany **Caffeine blocks the delayed K outward current of molluscan neurons.** Brain Research. 211(2):480-484, 1981.

Extracellular application of caffeine inhibited the delayed potassium (K) outward current of Aplysia neurons in a dose dependent manner without changing the kinetics. Half maximal blockade was obtained 1 to 2 minutes after application of 16mM caffeine. Intracellular injection of caffeine had an almost immediate blocking effect. Results suggest that the blocking site is on or close to the inner surface of the cellular membrane. 23 references. (Author abstract modified)

003835 Hersh, Louis B. Dept. of Biochemistry, University of Texas Health Science Center, 5323 Harry Hines Boulevard, Dallas, TX 75235 **Inhibition of aminopeptidase and acetylcholinesterase by puromycin and puromycin analogs.** Journal of Neurochemistry. 36(4):1594-1596, 1981.

Puromycin analogs in which the o-methyl-L-tyrosine moiety was substituted by a number of amino acids were examined as inhibitors of the puromycin sensitive rat brain aminopeptidase and bovine erythrocyte acetylocholinesterase. In the case of the aminopeptidase, the structure and stereochemistry of the amino acid substituent were important factors in determining inhibitor effectiveness. In the case of the acetylcholinesterase reaction, the aminonucleoside of puromycin was nearly as effective an inhibitor as puromycin itself, with little effect dependent on the nature of stereochemistry of the amino acid. 19 references. (Author abstract)

003836 Hertz, L.; Richardson, J. S.; Mukerji, S. Dept. of Pharmacology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Doxepin, a tricyclic antidepressant, binds to normal, intact astroglial cells in cultures and inhibits the isoproterenol-induced increase in cyclic AMP production.** Canadian Journal of Physiology and Pharmacology. 58(12):1515-1519, 1980.

The binding of doxepin, a tricyclic antidepressant which is not a potent inhibitor of either monoamine uptake or monoamine oxidation, to normal, intact astroglial cells in cultures was examined. Doxepin binding to intact astrocytes in primary cultures is competitively displaceable by excess cold doxepin. The binding is pronounced (Bmax = 27nmol/mg protein), but the affinity is rather low (KD = 20mcM). The binding is inhibited by other antidepressants (amitriptyline, desipramine, tranylcypromine, iprindole) and propranolol, but not by isoproterenol. Doxepin effectively counteracts the increase in the production of cyclic AMP evoked by isoproterenol. 21 references. (Author abstract modified)

003837 Herz, A.; Duka, T.; Gramsch, C.; Hollt, V.; Osborne, H.; Przewlocki, R.; Schulz, R.; Wuster, M. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, D-8000 Munchen 40, West Germany **Pharmacologic manipulation of brain and pituitary endorphin content and release.** Advances in Biochemical Psychopharmacology. 22:323-333, 1980.

Studies involving pharmacologic manipulation of brain and pituitary endorphin content and release are described. These include: in vitro experiments concerning the mechanism of release and the possible modulation by drugs at the cellular level; and in vivo experiments with acute and chronic drug administration. Benzodiazepines induced opposite changes in the enkephalin levels in the striatum and in the hypothalamus in vivo, but not in vitro. It is noted that although drug treatment may be used as a tool to manipulate endorphin levels, in most cases these changes are not linked with gross behavioral alterations. Methodological implications are discussed. 34 references.

003838 Hevor, Tobias; Gayet, Jacques. Gayet: Laboratoire de Physiologie Generale, Universite de Nancy I, C.O. 140, F-54037 Nancy Cedex, France **Stimulation of fructose-1,6-biphosphatase activity and synthesis in the cerebral cortex of rats submitted to the convulsant methionine sulfoximine.** Journal of Neurochemistry. 36(3):949-958, 1981.

The effect of the convulsant methionine sulfoximine (MSO) on fructose-1,6-biphosphatase (FBPase) activity in male Sprague-Dawley rat cerebral cortex was examined. FBPase from cortex was purified by substrate elution from phosphocellulose followed by Sephadex-G-200 column filtration. Expressed as mcmol fructose-1,6-biphosphate hydrolyzed per gram brain tissue wet weight per minute, FBPase activity doubled 24 hours after i.p. injection of 100mg/kg MSO. The rate of incorporation of (1-14C)valine into brain FBPase showed an even larger increase. The number of immunotitrable FBPase molecules also increased after MSO, due to an increase in the synthesis of the enzyme. 47 references. (Author abstract modified)

003839 Hill, D. R.; Bowery, N. G. Dept. of Pharmacology, St. Thomas's Hospital Medical School, London SE1 7EH, England **3H-baclofen and 3H-GABA bind to bicuculline-insensitive GABAB sites in rat brain.** Nature 290(5802):149-152, 1981.

The high affinity saturable binding of 3H-baclofen and 3H-GABA to the bicuculline insensitive GABAB site in rat brain is reported. It is noted that the presence of a novel receptor for the neurotransmitter GABA on peripheral autonomic nerve terminals and in mammalian brain slices has been described recently. This receptor differs from the classical GABA site as it is unaffected by recognized GABA antagonists such as bicuculline and is not sensitive to the majority of accepted GABA mimetics such as 3-aminopropanesulphonic acid or isoguvacine. It is proposed that the classical site be designated GABAA and the novel site as the GABAB receptor. Results support the concept of a novel GABA receptor within the mammalian brain and show that GABA and baclofen can compete for the same recognition site. 20 references. (Author abstract modified)

003840 Hiller, Jacob M.; Simon, Eric J. Dept. of Psychiatry, New York University Medical Center, New York, NY 10016 **Specific, high affinity (3H)ethylketocyclazocine binding in rat central nervous system: lack of evidence for kappa receptors.** Journal of Pharmacology and Experimental Therapeutics. 214(3):516-519, 1980.

The binding properties and distribution of the tritiated benzomorphan, (3H)ethylketocyclazocine, were studied in rat CNS. Specific binding was saturable and represented 75% to 90% of total binding. Scatchard analysis was consistent with the existence of two classes of binding sites with Kd values of 0.5nM and 10.5nM, respectively. Ethylketocyclazocine binding was increased in the presence of sodium chloride. This characteristic resembles that of opiate antagonists rather than that of other agonists. The distribution of binding in rat CNS followed closely that seen with other opiate ligands. The IC50 values of various opioid agonists and antagonists for competition with (3H)ethylketocyclazocine correlated well with their IC50 values for competition with (3H)naloxone. This evidence does not lend support to the existence of a separate kappa receptor in rat CNS. 23 references. (Author abstract)

003841 Hillier, Keith; Templeton, Wilma W. Southampton University, Medical & Biological Sciences Bldg., Bassett Crescent East, Southampton S09 3TU, England **Regulation of noradrenaline overflow in rat cerebral cortex by prostaglandin E2.** British Journal of Pharmacology. 70(3):469-473, 1980.

The effects of prostaglandin (PG) and PG inhibitors on the potassium evoked overflow of 3H-noradrenaline (3H-NA) from female Wistar rat cerebral cortex slices were examined. Evoked overflow was reduced by PGE2 and increased by the PG synthesis inhibitor indomethacin or the PG receptor antagonist SC-19220. The inhibition of 3H-NA overflow by PGE2 was dose dependently antagonized by SC-19220. Results indicate that PGE2 modulates NA release in rat cerebral cortex in vitro. 27 references. (Author abstract modified)

003842 Hinoki, M.; Nakanishi, K.; Ito, S. Dept. of Otolaryngology, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto, Japan, 606 **Nystagmic responses of hippocampal origin with reference to excitability of cholinergic and adrenergic components involved in the hippocampus of rabbits.** Agressologie. 20(1):11-18, 1979.

Using chemical substances relevant to neurotransmission in the central nervous system, nystagmic responses of hippocampal origin were studied in rabbits. Adrenaline or carbachol at a rate of .005mg/kg of bodyweight was injected into the brain. Changes in reaction to the substances were examined before and after repeated electric stimulation of the brain. Results show two types of nystagmic responses of hippocampal origin, prompt and delayed. The former type of response is elicited soon after injection of carbachol into the hippocampus of a normal rabbit. The prompt response is a horizontal nystagmic response directed to the side of the injection and is accompanied by an EEG arousal state. The latter type of nystagmic response is a horizontal response directed to the right and the left, and it appears with rather long latency. The delayed response is elicited in a normal rabbit on the basis of a rebound in the EEGs, brought about by injection of carbachol into the hippocampus; it is also elicited in rabbits with repeated electric stimulations of the hippocampus on the basis of a rebound in the EEGs, brought about by injection of adrenaline into the same brain. Repeated electric stimulations of the hippocampus results in alterations of the two kinds of nervous components described above. Thus, after electric stimulation, the two types of nystagmic responses barely can be induced with an injection of carbachol. In contrast, nystagmic response of the delayed type is easily induced with an injection of adrenaline. 7 references. (Journal abstract modified)

003843 Hirai, K.; Koketsu, K. Dept. of Physiology, Kurume University School of Medicine, Kurume 830, Japan **Presynaptic regulation of the release of acetylcholine by 5-hydroxytryptamine.** British Journal of Pharmacology. 70(3):499-500, 1980.

The effect of 5-hydroxytryptamine (5-HT) on the release of acetylcholine (ACh) from bullfrog sympathetic preganglionic nerve terminals and frog sciatic nerve terminals was studied with intracellular microelectrodes. Low concentrations of 5-HT (1 to 30 mcM) facilitated ACh release, but higher concentrations of 5-HT (100 to 1000 mcM) depressed ACh release at preganglionic and motor nerve terminals. Results suggest that 5-HT may play a role in regulating cholinergic transmission in general. 3 references. (Author abstract modified)

003844 Hirsch, James D. Dept. of Biological Research, G. D. Searle & Co., P.O. Box 5110, Chicago, IL 60680 **Regional changes in (3H)diazepam binding in the brains of mice after removal of the olfactory bulbs.** Experimental Neurology. 72(1):91-98, 1981.

(3H)Diazepam binding was assayed 3 weeks after surgery in 13 brain regions derived from sham operated and bilaterally olfactory bulbectomized mice. In bulbectomized mice, (3H)diazepam binding was elevated 30% in the frontal cortex and 24% in the thalamus but decreased 26% in the striatum and 28% in the midbrain. These changes represent alterations in the number of binding sites. No binding changes were observed in the olfactory tubercle, amygdala, piriform cortex, olfactory peduncle, hypothalamus, hippocampus, colliculi, cerebellum, or pons/medulla of bulbectomized animals. These results are compared with the effects of other types of brain lesions on the brain benzodiazepine receptor, and are possibly related to the altered sensitivity of bulbectomized mice to benzodiazepines and convulsants. 30 references. (Author abstract)

003845 Hoffman, W. E.; Weet, J. F.; Phillips, M. I.; Schmid, P. G. Dept. of Medical Physiology, Texas A&M University, College Station TX 77843 **Central effects of angiotensin II in water and saline loaded rats.** Neuroendocrinology. 28:289-296, 1979.

Experiments were performed to evaluate the role of antidiuretic hormone (ADH) release versus neurogenic mechanisms in the antidiuretic responses to intracerebroventricular (IVT) angiotensin II (AII) injections. Median eminence lesions used to block ADH release abolished antidiuretic effects but only attenuated pressor responses to IVT AII infusions. Pretreatment with an intravenous infusion of ADH antibody had a similar effect. Central administration of AII in water and saline loaded rats produced no change in effective renal plasma flow or glomerular filtration rate. Natriuretic and kaliuretic responses to IVT AII injections were similar to those observed in intravenous ADH infusions. These data are consistent with the suggestion that antidiuresis and osmotic excretion observed after IVT AII injections in rats are the result of ADH release, and that neurogenic mechanisms play a greater role in the blood pressure but not in the antidiuretic responses. (Journal abstract modified)

003846 Hollt, V.; Haarmann, I.; Przewlocki, R.; Jerlicz, M. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, D-8000 Munchen 40, West Germany **Long-term treatment of rats with morphine decreases in vitro biosynthesis in and release of beta-endorphin from intermediate/posterior lobes of pituitary.** Advances in Biochemical Psychopharmacology. 22:399-407, 1980.

The effects of long-term treatment of rats with morphine on in vitro biosynthesis in and release of beta-endorphin from intermediate/posterior lobes of pituitary were investigated. The experimental system of isolated rat intermediate/posterior lobes in vitro allowed for simultaneous investigation of beta-endorphin release, synthesis of its precursor molecule, and the processing of this precursor into beta-lipotropin and beta-endorphin. The decreased in vitro release of beta-endorphin observed is indicative that the depressed levels of beta-endorphin in the intermediate/posterior lobes seen following long-term morphine treatment are probably not due to an increased release. In addition to a decreased biosynthesis of beta-endorphin, the data indicate a slight delay in the posttranslational processing of the precursor into beta-lipotropin and beta-endorphin in the pituitary lobes of the morphinized rats. Results are discussed in relation to mechanisms of opiate addiction. 16 references.

003847 Holmstedt, Bo; Nordgren, Ingrid. Swedish Medical Research Council, Karolinska Institutet, Stockholm, Sweden **Stable isotopes used in studies of metrifonate.** In: Klein, E. Stable isotopes. New York, Academic Press, 1979. (p. 443-451).

The transformation of metrifonate in vivo by the use of stable isotopes was examined. Chemical formation of dichlorvos (2,2-dichlorovinyl dimethyl phosphate) was found to occur in mouse brain after i.p. injection of metrifonate. A mass fragmentographic technique was used. Different isotopic variants were used both as internal standards and to compensate for dichlorvos formed during the workup procedure. The dichlorvos formed in vivo was found to have its maximal concentration a few minutes after the maximum of the metrifonate itself. It is concluded that metrifonate acts as a slow release formulation in the body giving rise to dichlorvos nonenzymatically. This circumstance at least partly explains its efficacy in the treatment of schistosomiasis. 22 references. (Author abstract modified)

003848 Honore, Tage; Lauridsen, Jorn; Krogsgaard-Larsen, Povl. Royal Danish School of Pharmacy, Dept. of Chemistry BC, Universitetsparken 2, DK-2100 Copenhagen O, Denmark **Ibotenic acid analogues as inhibitors of (3H)glutamic acid binding to cerebellar membranes.** Journal of Neurochemistry. 36(3):1302-1304, 1981.

The binding of L-(3H)glutamic acid to Sprague-Dawley rat cerebellar membranes prepared with or without preincubation at 37 degrees followed by washing was studied. The specificity of the binding of ibotenic acid analogues did not differ in the two preparations. The order of potency of ibotenic acid analogues as inhibitors of L-(3H)glutamic acid binding differed from that found in vivo, suggesting the binding sites differ from the physiological glutamic acid receptor. 18 references. (Author abstract modified)

003849 Hosford, David A.; Haigler, Henry J. Dept. of Pharmacology, Emory University, Atlanta, GA 30322 **Morphine and methionine-enkephalin: different effects on spontaneous and evoked neuronal firing in the mesencephalic reticular formation of the rat.** Journal of Pharmcology and Experimental Therapeutics. 213(2):355-363, 1980.

The effects of morphine and methionine-enkephalin (met-enk) on spontaneous neuronal firing and on firing evoked by a nociceptive stimulus (evoked firing) were investigated via microiontophoretic techniques. Morphine and met-enk produced one of the three following patterns of effects on single units in the mesencephalic reticular formation: 1) morphine but not met-enk blocked evoked firing; 2) met-enk but not morphine blocked evoked firing; and 3) both morphine and met-enk blocked evoked firing. There appear to be differences in cell size and location which are associated with different effects of the drugs. The difference in the effects of the drugs on evoked firing cannot be explained by differences in transport number, diffusion, or degradation of the drugs, nor by different locations of the drug ejection barrels. Naloxone, administered intravenously or microiontophoretically, antagonized the drug-induced blockade. The effects of morphine and met-enk on spontaneous firing did no correlate with their effect on evoked firing. Furthermore, in the majority of cases, the effects of morphine and met-enkephalin on spontaneous firing were not the same. These data indicate that there may be more than one type of opiate receptor in the mesencephalic reticular formation. 34 references. (Author abstract modified)

003850 Hotchkiss, Adair J.; Gibb, James W. Gibb: Dept. of Biochemical Pharmacology and Toxicology, University of Utah, Salt Lake City, UT 84112 **Long-term effects of multiple doses of methamphetamine on tryptophan hydroxylase and tyrosine hydroxylase activity in rat brain.** Journal of Pharmacology and Experimental Therapeutics. 214(2):257-262, 1980.

The long-term effects of multiple doses of methamphetamine (METH) on tryptophan hydroxylase (TPH) and tyrosine hydroxylase activity in rat brain were investigated. TPH activity was measured in various rat brain regions after administering large doses of METH. After four sequential doses of METH, given every 6 hours, TPH activity was decreased in both the neostriatum and hippocampus. The depression of enzyme activity persisted for at least 30 days. When compared with the depression of neostriatal tyrosine hydroxlyase activity, the depression of neostriatal and hippocampal TPH activity occurred sooner and was more pronounced. The depression of TPH activity was dependent on the number of doses and the amount of drug administered. Agents which prevent the METH-induced decrease of neostriatal tyrosine hydroxylase activity, i.e., haloperidol, alpha-methyl-p-tyrosine, and GABA transaminase inhibitors, also prevented the decrease in TPH activity caused by METH. In addition, fluoxetine, an inhibitor of 5-hydroxytryptamine reuptake, prevented the METH-induced decrease in neostriatal and hippocampal TPH activity but did not alter the decrease in neostriatal tyrosine hydoxylase activity. 20 references. (Author abstract modified)

003851 Hunt, P.; Clements-Jewery, S. Centre de Recherches Roussel-Uclaf, F-93230 Romainville, France **A steroid derivative, R 5135, antagonizes the GABA/benzodiazepine receptor interaction.** Neuropharmacology. 20(4):357-361, 1981.

The steroid derivative R-5135 (3alpha-hydroxy-16-imino-5beta-17-aza-androstan-11-one) showed high affinity for GABA and glycine receptors in vitro and displaced 3H-diazepam binding from the benzodiazepine receptor in male Sprague-Dawley rat cortical membranes. The high affinity component of R-5135 inhibition disappeared when endogenous GABA was reduced by extensive washing of the membrane preparation and reappeared when GABA was reintroduced. R-5135 was 500 times more active than was bicuculline as an antagonist of GABA stimulation of 3H-diazepam binding. 23 references. (Author abstract modified)

003852 Hussein, L.; Goedde, H. W. Goedde: Institut fur Humangenetik, Universitat Hamburg, Butenfeld 32, D-2000 Hamburg 54, West Germany **Studies on the kinetic properties of tryptophan hydroxylase of rabbit mesencephalon and pons medulla: effect of long-term treatment with neuroleptics and antidepressants.** Arzneimittel-Forschung. 30(10):1704-1708, 1980.

Tryptophan hydroxylase activity was measured in mesencephalon and pons medulla of rabbits receiving reserpine or other neuroleptics which are chemically related to phenothiazines (chlorpromazine), dibenzothiazepine (imipramine), dibenzobicyclooctadiene (maprotiline), dibenzothiepines (methiothepin), butyrophenones (haloperidol), and tetrahydroisoquinolines (nomifensine). Chronic intramuscular administration of imipramine and nomifensine increased the affinity of mesencephalic tryptophan hydroxylase for tryptophan. The injection of chlorpromazine increased the enzyme activity significantly in comparison to control values. 24 references. (Author abstract)

003853 Huth, P. J.; Schmidt, M. J.; Hall, P. V.; Fariello, R. G.; Shug, A. L. Shug: Metabolic Research Laboratory, William S. Middleton Memorial Veterans Hospital, 2500 Overlook Terrace, Madison, WI 53705 **The uptake of carnitine by slices of rat cerebral cortex.** Journal of Neurochemistry. 36(2):715-723, 1981.

The properties of carnitine uptake were studied in male Holtzman rat brain slices. Results were consistent with the presence of a relatively low affinity, high capacity, active transport system associated with the plasma membrane. L-carnitine uptake was competitively inhibited by GABA, suggesting that the two compounds may interact at a common carrier site and that carnitine may modulate GABA transport. Carnitine uptake was sodium dependent, but did not require potassium or calcium ions. 41 references. (Author abstract modified)

003854 Hwang, Eunyong Chung; Van Woert, Melvin H. Dept. of Neurology, Mount Sinai School of Medicine, Fifth Ave. and 100th St., New York, NY 10029 **Comparative effects of substituted phenylethylamines on brain serotonergic mechanisms.** Journal of Pharmacology and Experimental Therapeutics. 213(2):254-260, 1980.

A series of substituted phenylethylamines were examined for their relative potencies to: 1) release and inhibit accumulation of labeled serotonin in brain synaptosomes; 2) complete with serotonin receptor binding; and 3) induce the serotonin syndrome in mice. In general, the relative potencies of the phenylethylamine derivatives to procude the serotonin syndrome in mice. In general, the relative potencies of the phenylethylamine derivatives to produce the serotonin syndrome did not correlate well with their effects on synaptosomal uptake or release or serotonin or serotonin receptor binding. However, para chloro substitution was more effective than meta or ortho chlorophenylethylamine and para methoxy substitution more effective than ortho methoxyphenylethylamine for (3H)serotonin uptake inhibition and release and induction of the serotonin syndrome. The ability of phenylethylamine derivatives to release preferentially (3H)serotonin in vitro without damaging serotonin neurons and to consistently and rapidly produce the serotonin syndrome in vivo should make these compounds useful pharmacological tools for investigating brain serotonin matabolism. 26 references. (Author abstract modified)

003855 Hyslop, Deborah K.; Taylor, Duncan P. Biologic Research, Mead Johnson Pharmaceutical Division, Evansville, IN 47721 **The interaction of trazodone with rat brain muscarinic cholinoceptors.** British Journal of Pharmacology. 71(2):359-361, 1980.

The muscarinic receptor binding of trazodone, a new nontricyclic antidepressant, was examined. Inhibition of 3H-quinuclidinyl benzilate binding to washed membranes from male Sprague-Dawley rat hippocampus was used to estimate anticholinoceptor activity. Trazodone was at least two orders of magnitude weaker than the tricyclic antidepressants, which possess from 0.001 to 0.005 the potency of atropine in this assay. 10 references. (Author abstract modified)

003856 Ichida, Seiji; Okada, Kozo; Terao, Motome. Dept. of Toxicology, Faculty of Pharmacy, Kinki University, Kowakae, Higashi-Osaka 577, Japan **Effect of verapamil on 45Ca uptake by synaptosomes.** Japanese Journal of Pharmacology. 30(2):207-211, 1980.

Verapamil and manganese ion (Mn) inhibited the uptake of labeled calcium (45Ca) in male Sprague-Dawley synaptosomes incubated in a high potassium medium (60 mM), but not in a medium containing only 5 mM potassium. A decrease in the calcium concentration in the reaction medium from 1 mM to 0.1 mM decreased the medium inhibitory concentration for Mn from 1.7 mM to 0.2 mM, but did not significantly alter inhibition induced by verapamil. These findings indicate that verapamil and Mn act through different mechanisms to inhibit the potassium stimulated uptake of 45Ca. 18 references. (Author abstract modified)

003857 Iorio, Louis C.: Latranyi, Miklos; Heath, Eugene; Barnett, Allen. Biological Research, Schering Corp., Bloomfield, NJ 07003 **Blockade by l-lysine of non-narcotic analgesics.** Journal of Pharmacology and Experimental Therapeutics. 213(3):445-449, 1980.

The antinociceptive effects of the nonnarcotic analgesics clonixin, flunixin, acetylsalicyclic acid, aminopyrine, and phenylbutazone in the male CD rat yeast paw test were blocked by l-lysine. Lysine did not alter plasma or brain levels of flunixin or the binding of flunixin to plasma protein. The l-lysine blockade was not altered by l-arginine or l-ornithine, which compete with l-lysine for a common transport system; this finding suggests the l-lysine blockade was predominantly peripheral. The l-lysine blockade was not reversed by 5-hydroxytryptophan or fluoxetine, indicating the l-lysine blockade does not involve endogenous serotonin. In contrast to its effect on nonnarcotic analgesics, l-lysine potentiated the antinociceptive effects of morphine. 17 references. (Author abstract modified)

003858 Iwamoto, Edgar T. Dept. of Pharmacology, University of Kentucky, Lexington, KY 40536 **Studies on axonal transport in dopaminergic neurons: effect of neuropharmacologic lesions.** Life Sciences. 28(19):2179-2186, 1981.

Axonal transport of tritiated protein to the nucleus accumbens, olfactory tubercle, septal region, caudate nucleus, and hypothalamic region was studied in male Sprague-Dawley rats after unilateral injection of 3H-lysine into the substantia nigra. Results indicate that axonal transport of protein in dopamine containing systems is dependent upon the site of injection of labeled precursor and the integrity of a 6-hydroxydopamine sensitive pathway. Transport was sensitive to inhibitors of microtubule assembly and protein synthesis but not to intrastriatal kainic acid lesions. 16 references. (Author abstract modified)

003859 Jancso, Gabor; Kiraly, Elizabeth. Dept. of Anatomy, University Medical School, 6701 Szeged, P. O. B. 512, Hungary **Sensory neurotoxins: chemically induced selective destruction of primary sensory neurons.** Brain Research. 210(1-2):83-89, 1981.

Neonatal treatment with capsaicin or with some of its pungent congeners induced selective degeneration of type-B sensory ganglion cells in rats. The distribution pattern of axon terminal degeneration within the spinal cord and brainstem after high doses of capsaicin congeners was similar to that observed after capsaicin itself. The neurotoxic potency of capsaicin congeners, unlike their desensitizing activity, was closely related to the sensory irritant property of the compounds. It is suggested that the primary sensory neurons degenerating after neonatal administration of these capsaicin congeners are substance-P containing primary sensory neurons involved in the transmission of nociceptive impulses. 19 references. (Author abstract modified)

003860 Jav, Jaak; Hedlund, Britta; Bartfai, Tamas. Dept. of Organic Chemistry, Tartu University, Estonian SSR, USSR **Isomerization of the muscarinic receptor-antagonist complex.** Journal of Biological Chemistry. 254(13):5595-5598, 1979.

The mechanism of binding of two antagonists, 3-quinuclidinyl benzilate and N-methyl-4-piperidinyl benzilate, to the muscarinic receptor was studied. The pseudo first order rate constant of association showed a hyperbolic dependence on the concentration of the antagonist(s), indicating that the interaction involves two equilibria. The first binding equilibrium is reached rapidly and is characterized by dissociation constants 2.7nM and 6.7 nM in phosphate buffer for 3-quinuclidinyl benzilate and N-methyl-4-piperidinyl benzilate, respectively. The first binding equilibrium is followed by a slower isomerization step of the receptor/antagonist complex. The equilibrium constants for the isomerization step of the complex for both ligands were about 0.15. The overall constant of binding obtained as the product of the above constants shows good agreement with the results of equilibrium binding studies. 14 references. (Author abstract)

003861 Jensen, Robert A.; Martinez, Joe L., Jr.; McGaugh, James L.; Messing, Rita B.; Vasquez, Beatriz J. Dept. of Psychobiology, University of California, Irvine, CA 92664 **The psychobiology of aging.** In: Maletta, G.J., The aging nervous system. New York, Praeger, 1980. (p. 110-125).

The psychobiology of aging is examined in a report of research done with rats. The studies reviewed indicate that the memory deficits seen in aged animals are task specific and do not reflect generalized impairment, a finding in agreement with many studies conducted with aged humans. The impaired retention seen in the inhibitory avoidance task in the old rats demonstrates either that the initial level of acquisition strength is lower in these animals or that their rate of forgetting is greater. The data also indicate that there is comparable CNS degeneration in rats and that the consequence of this destruction is a decrease in the capacity of neurons to interact with one another. The appearance of these deficits is associated chronologically with both biochemical and behavioral changes. Basic age related differences in opiate receptor numbers and affinities that most probably relate in some way to the behavioral changes in the aged are noted. Relationships between the pharmacological basis of action of a drug and its neural substrate are related to behavioral differences between young and aged animals. 54 references.

003862 Jhamandas, K.; Elliott, J. Dept. of Pharmacology, Faculty of Medicine, Queen's University, Kingston, Ontario, Canada K7L 3N6 **Investigation of action of enkephalin on the spontaneous and evoked release of acetylcholine from rat cortical and striatal slices.** British Journal of Pharmacology. 71(1):211-217, 1980.

The effects of two synthetic enkephalins, D-Ala2-Met5-enkephalinamide (DALA) and D-Ala2-MePhe4-Met5-(O)-ol-enkephalin (33,824), on the spontaneous and stimulated release of acetylcholine (ACh) from male Sprague-Dawley rat cortical and striatal slices were studied. Spontaneous cortical ACh release was moderately increased by DALA, but not by 33,824. Neither enkephalin affected the release of cortical ACh induced by high potassium (25mM) or veratridine (20mcM). DALA had no effect on spontaneous ACh release from striatal slices or on striatal ACh release in the presence of potassium (25mM), veratridine (5mcM), or ouabain (10mcM); 33,824 slightly enhanced veratridine evoked release, but had no other effects on striatal ACh release. It is suggested that enkephalins have no significant action on ACh release from the cortex or striatum in vitro; their action on cortical ACh release in vivo may be exerted at a subcortical level. 25 references. (Author abstract modified)

003863 Jhamandas, Khem; Sutak, Maaja. Dept. of Pharmacology, Queen's University, Kingston, Ontario, Canada K7L 3N6 **Action of enkephalin analogues and morphine on brain acetylcholine release: differential reversal by naloxone and an opiate pentapeptide.** British Journal of Pharmacology. 71(1):201-210, 1980.

Intraventricular administration of Met-enkephalin, Leu-enkephalin, D-Ala2-Met5-enkephalinamide (DALA) or D-Ala2-D-Leu5-enkephalin (DALEU) produced a dose related inhibition of cortical acetylcholine (ACh) release in Sprague-Dawley rats in vivo. Met-enkephalin and Leu-enkephalin were similar in potency and time course; DALA and DALEU were more potent and had longer durations of action. Systemic injection of D-Met2-Pro5-enkephalinamide and D-Ala2-MePhe4-Met5(0)-ol-enkephalin produced a sustained inhibition of cortical ACh release. Systemic administration of naloxone reversed the effects of the enkephalins and their analogues, but D-Met2-Pro5-enkephalinamide was relatively resistant to naloxone. Intraventricular doses of D-Ala2-D-Ala3-Met5-enkephalinamide (TAAPM) that did not influence basal ACh release were able to block or reverse the inhibitory effect of morphine on ACh release. TAAPM did not block the effect of chlorpromazine under similar conditions and failed to reverse the inhibition of ACh release induced by systemically injected D-Met2-Pro5-enkephalinamide. Results suggest that enkephalinergic and cholinergic mechanisms may interact in the CNS. 25 references. (Author abstract modified)

003864 Jiang, Z. G.; Chelack, B. J.; Phillis, J. W. Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Effects of morphine and caffeine on adenosine release from rat cerebral cortex: is caffeine a morphine antagonist.** Canadian Journal of Physiology and Pharmacology. 58(12):1513-1515, 1980.

The effects of caffeine on the morphine evoked purine release from rat cerebral cortex were investigated. Morphine enhances the efflux of labeled adenosine and its derivatives from the rat cerebral cortex. Caffeine does not alter either basal purine efflux rates or the enhanced efflux elicited by morphine. Therefore, the antagonism by caffeine of morphine evoked inhibition of acetylcholine (ACh) release from the cerebral cortex is unlikely to be the result of an action of caffeine on the opiate receptor. It is suggested that the caffeine effect is due to an antagonism of the inhibitory effect of released adenosine on ACh release. Thus, the depression of ACh release by morphine may involve a purinergic step. 10 references. (Author abstract modified)

003865 Jobe, Phillip C.; Brown, R. Don; Dailey, John W. Dept. of Pharmacology and Therapeutics, Louisiana State University School of Medicine, P.O. Box 33932, Shreveport, LA 71130 **Effect of Ro 4-1284 on audiogenic seizure susceptibility and intensity in epilepsy-prone rats.** Life Sciences. 28(18):2031-2038, 1981.

The effects of CNS monoamine depletion on audiogenic seizure (AGS) susceptibility and intensity were studied in two types of Sprague-Dawley derived rats: 1) the progeny of a nonsusceptible strain (controls); and 2) the nonsusceptible progeny of epilepsy prone (audiogenic seizure susceptible) parents (NSPSP). Forty five minutes after injection of the benzoquinolizine Ro 4-1284, a significant fraction of the NSPSP developed AGS susceptibility, whereas the incidence in control Ss was not significant. AGS intensity was also significantly elevated 45 minutes and 19 days following Ro 4-1284 administration in NSPSP. In control Ss, there was a smaller, but significant elevation of seizure intensity only at the earlier time period. Both types of rats exhibited marked depletion of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) in all six areas of CNS examined. In the NSPSP, a significant incidence of seizure susceptibility was retained as long as 19 days after Ro 4-1284 administration, despite the complete depletion of monoamine stores. These observations suggest that CNS monoaminergic neurons function as determinants of AGS susceptibility and AGS intensity in animals which also carry some other genetically determined susceptibility factor(s). 17 references. (Author abstract modified)

003866 Johnson, Robert G.; Carty, Sally E.; Scarpa, Antonio. Scarpa: B-501 Richards Building, Dept. of Biochemistry and Biophysics, University of Pennsylvania, Philadelphia, PA 19104 **Accumulation of amantadine by isolated chromaffin granules.** Biochemical Pharmacology. 30(7):763-769, 1981.

The accumulation of amantadine and the effect of this pharmacologic amine upon the magnitude of the transmembrane proton gradient (delta pH) and of the transmembrane potential gradient (delta psi) were investigated in bovine adrenal chromaffin granules isolated in isotonic sucrose. The addition of amantadine to well buffered suspensions of granules at pH 7.0 resulted in a dose related alkalinization of the granule interior. Similar results were obtained with equivalent external concentrations of ammonia. When the time resolved influx of labeled amines into the granules was studied radiochemically, using low external amine concentrations, the accumulation of (3H)amantadine was quite similar to that of (14C)methylamine with regard to rate and extent over a wide range of magnitudes of the transmembrane proton gradient. Unlike biogenic amine accumulation into the chromaffin granule, which is driven by both transmembrane proton and potential gradients, the accumulation of (3H)amantadine was not stimulated by the existence of a transmembrane potential, nor was it inhibited by reserpine. Moreover, low concentrations of amantadine did not competitively inhibit biogenic amine accumulation in the isolated granules. Results indicate that amantadine can distribute across the membrane of chromaffin granules according to the magnitude of the endogenous delta pH, and suggest that in vivo amantadine may be concentrated and stored as a pharmacologic agent in amine containing granules. 25 references. (Author abstract modified)

003867 Johnston, G. A. R.; Hailstone, M. H.; Freeman, C. G. Dept. of Pharmacology, University of Sydney, N. S. W. 2006, Australia **Baclofen: stereoselective inhibition of excitant amino acid release.** Journal of Pharmacy and Pharmacology. 32(3):230-231, 1980.

The effects of baclofen on the release of labeled D-aspartate and GABA from rat cerebral cortex and cat spinal cord slices were examined. Results showed that (-)-baclofen (4mcM) inhibited the evolved release of preloaded 3H-D-aspartate by about 50%; ()-baclofen was inactive at 4mcM and weakly potentiated D-aspartate release at 10mCM. Neither isomer altered the release of 3H-GABA. 16 references.

003868 Jones, Stephen W.; Sumikawa, Katumi. 146 Clark Hall, c/o Applied Physics, Cornell University, Ithaca, NY 14853 **Quinuclidinyl benzilate binding in house fly heads and rat brain.** Journal of Neurochemistry. 36(2):454-459, 1981.

The binding of 3-quinuclidinyl benzilate (QNB) to house fly heads was similar in affinity and pharmacology to that in rat brain. The house fly site bound (-)QNB preferentially, as do classic muscarinic receptors. The binding was sensitive to other muscarinic agonists and antagonists. Nicotinic drugs were no more effective on the house fly site than on the rat brain muscarinic receptor. Results suggest that the house fly QNB site is a classic muscarinic acetylcholine receptor. 17 references. (Author abstract modified)

003869 Juel, C. Zoophysiological Laboratory B, August Krogh Institute, 13 Universitetsparken, DK-2100 Copenhagen O, Denmark **Presynaptic modulation of synaptic transmission in Helix Pomatia: the effects of serotonin and dopamine antagonists.** Neuropharmacology. 20(4):323-326, 1981.

Presynaptic serotonin (5-HT) and dopamine (DA) receptors in Helix pomatia were characterized. The 5-HT antagonists tryptamine, 7-methyltryptamine, morphine, atropine, and methysergide decreased transmitter mobilization; while 5-methoxy-gramine, a selective inhibitor of hyperpolarizing 5-HT responses, had no effect. The dopamine antagonists curare, chlorpromazine, and haloperidol decreased transmitter mobilization, while ergometrine, flupenthixol, promthazine, and 6-hydroxydopamine induced a small increase. The use of the Helix nervous system in studies of the mechanism of action of antipsychotic drugs is discussed. 21 references. (Author abstract modified)

003870 Juorio, A. V. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, S7N OXO, Canada **Effects of molindone and fluphenazine on the brain concentration of some phenolic and catecholic amines in the mouse and the rat.** British Journal of Pharmacology. 70(3):475-480, 1980.

Dopamine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, p-tyramine, and m-tyramine concentrations were measured in the striatum of male Swiss mice and male Wistar rats after subcutaneous injection of molindone or fluphenazine. Low doses of molindone (1 to 10mg/kg) reduced striatal p-tyramine, increased m-tyramine, and increased dopamine turnover. Similar effects were seen after all doses of fluphenazine (0.1 to 5mg/kg). A high dose of molindone (100mg/kg) had opposite effects on tyramines and dopamine metabolism. Higher doses of molindone (20 to 100mg/kg) also increased hypothalamic concentrations of p-octopamine and m-octopamine in mice. All doses of fluphenazine reduced hypothalamic p-octopamine. Results suggest that molindone acts as a blocker or partial agonist of dopamine receptor sites and support the proposed reciprocal relation between dopamine and tyramine. 29 references. (Author abstract modified)

003871 Kamata, Katsuo; Kamata, Michiru; Ino, Hiroya; Kameyama, Tsutomu. Dept. of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Change in catecholamine-sensitive Na,K-ATPase activity in the rat striatum microsomes following electrolytic or 6-hydroxydopamine-induced lesions of dopaminergic neurons.** Japanese Journal of Pharmacology. 30(3):401-404, 1980.

Sodium and potassium stimulated adenosine triphosphatase (NA,K-ATPase) activity was measured in the striatum of male Wistar rats with unilateral lesions of the left substantia nigra made by microinjection of 6-hydroxydopamine or by electrolytic coagulation. Striatal Na,K-ATPase activity was markedly enhanced by dopamine or norepinephrine; isoproterenol was also active, but serotonin, carbachol, and GABA were inactive. Unilateral nigral lesions reduced the dopamine content in the ipsilateral striatum to 0 to 30% of that in the contralateral striatum or in intact striatum. The sensitivity of Na,K-ATPase to dopamine in the ipsilateral striatum was increased 2 days after surgery and continued to increase gradually until a maximum was reached 7 to 10 days after lesion. Results are discussed in relation to dopaminergic supersensitivity in caudate neurons. 19 references.

003872 Kamer, Russell S.; Turi, Anthony R.; Solomon, Paul R.; Kaplan, Lawrence J. Solomon: Dept. of Psychology, Williams College, Williamstown, MA 01267 **Increased mesolimbic dopamine binding following chronic haloperidol treatment.** Psychopharmacology. 72(3):261-263, 1981.

In a study of the effect of chronic neuroleptic treatment on mesolimbic dopamine receptor binding, male Sprague-Dawley rats were given haloperidol (0.5mg/kg), sodium phenobarbital (50mg/kg), or saline daily for 21 days. One week after the last injection, rats were sacrificed and the septi were removed from the 3H-dopamine binding assay. Haloperidol treatment resulted in a 52% increase in 3H-dopamine binding in the septum, whereas phenobarbital treatment caused no significant change. 12 references. (Author abstract modified)

003873 Kamp, Cylia W.; Morgan, William W. Dept. of Anatomy, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78283 **Some barbiturates enhance the effect of muscimol on dopamine turnover in the rat retina.** Journal of Pharmacology and Experimental Therapeutics. 213(2):332-336, 1980.

The effects of several barbiturates on the muscimol mediated reduction of the light evoked activation of dopamine (DA) turnover were tested. The decline in retinal DA content after alpha-methyl-p-tyrosine was used as an indication of turnover. Neither pentobarbital nor the low dosage of muscimol alone significantly altered the light evoked increase in retinal DA turnover. However, the combination of pentobarbital and muscimol significantly reduced the light mediated increase in DA turnover to a level below that normally observed in dark maintained animals. These results and other data provide evidence for a GABA potentiating component to the anesthetic and anticonvulsant mechanism of barbiturate action and the first neurochemical demonstration of barbiturate mediated potentiation of GABA agonist. 26 references. (Author abstract modified)

003874 Kan, J. P.; Benedetti, M. Strolin. Benedette: Centre de Recherche Delalande, 10, rue des Carrieres, F-92500 Rueil-Malmaison, France **Characteristics of the inhibition of rat brain monoamine oxidase in vitro by MD780515.** Journal of Neurochemistry. 36(4):1561-1571, 1981.

The inhibition of type-A and type-B monoamine oxidase (MAO-A, MAO-B) in rat forebrain crude membrane preparations by MD780515 was investigated in vitro with 5-hydroxytryptamine (5-HT) and beta-phenylethylamine as substrates. The inhibition of the high affinity binding of (3-H)harmaline, a specific marker of MAO-A, was also studied. MD780515 appeared to be a pure mixed MAO inhibitor of 5-HT deamination. The hypothesis that beta-phenylethylamine (PEA) can be deaminated by both forms of MAO was confirmed by biphasic inhibition curves of PEA obtained when MD780515, clorgyline, harmaline, and deprenyl were used as MAO inhibitors. It is concluded that MD780515 is a reversible, specific, and potent type-A MAO inhibitor. 30 references. (Author abstract modified)

003875 Kaufmann, Konrad. Max-Planck-Institut fur biophysikalische Chemie, D-34 Gottingen, West Germany **Inseparability of acetylcholinesterase and nerve excitation.** Neurochemistry International. 2(1/3):111-112, 1980.

It is proposed that acetylcholinesterase causes the movement of sodium and potassium ions toward equilibrium during nerve excitation. This proposition is consistent with the observed kinetics of acetylcholine (ACh) at unmodified membrane fragments. Conductivity increases for sodium and potassium ions can be observed after application of ACh onto blackfilm lipid membranes near the phase transition, as well as at cholinergic membranes where lipids are generally away from their phase transition temperature. It is concluded that unit channels at unmodified cholinergic membranes can be triggered by the microenvironment of acetylcholinesterase after application of the physiological agonist ACh. 14 references.

003876 Kayaalp, S. Oguz; Rubenstein, J. S.; Neff, N. H. Neff: Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Inhibition of dopamine D-1 and D-2 binding sites in neuronal tissue by ascorbate.** Neuropharmacology. 20(4):409-410, 1981.

The binding of radiolabeled dopamine (DA) and DA agonists to D-1 and D-2 receptor sites in rat neuronal membranes was inhibited by ascorbate in concentrations greater than 10mcM. Results suggest that DA agonist binding to neuronal tissue should be reevaluated, since most previous studies have been performed in the presence of 1 to 5mM ascorbate. 11 references. (Author abstract modified)

003877 Kayama, Yukihiko; Hsiao, Chie-Fang; Fukuda, Yutaka; Iwama, Kitsuya. Dept. of Neurophysiology, Institute of Higher Nervous Activity, Osaka University Medical School, Kita-ku, Osaka 530, Japan **Sensitivity to GABA of neurons of the dorsal and ventral lateral geniculate nuclei in the rat.** Brain Research. 211(1):202-205, 1981.

Ionotophoretic application of GABA to dorsal and ventral lateral geniculate (LGd and LGv) neurons in Sprague-Dawley rats readily suppressed spontaneous discharges in both types of neurons. Discharges evoked by optic nerve stimulation were suppressed as readily as spontaneous discharges in LGd neurons. In LGv neurons, however, evoked discharges were more resistant than spontaneous discharges to the effects of GABA. 133 references. (Author abstract modified)

003878 Kellar, Kenneth J.; Cascio, Caren S.; Butler, Judith A.; Kurtzke, Robert N. Dept. of Pharmacology, Georgetown University, Schools of Medicine and Dentistry, Washington, DC 20007 **Differential effects of electroconvulsive shock and antidepressant drugs on serotonin-2 receptors in rat brain.** European Journal of Pharmacology. 69(4):515-518, 1981.

The effects of chronic administration of electroconvulsive shock (ECS) and antidepressant drugs on brain serotonin-2 (5-HT2) receptors were investigated in male Sprague-Dawley rats. Chronic administration of amitriptyline, iprindol, or tranylcypromine decreased the binding of 3H-spiperone to 5-HT2 receptors in cerebral cortex homogenates. A single ECS had no significant effect on 3H-spiperone binding, but 3 to 12 days of ECS caused a progressive increase in the density of 5-HT2 receptors labeled by 3H-spiperone. 10 references. (Author abstract modified)

003879 Kenakin, Terry P. Dept. of Pharmacology, Burroughs Wellcome Co., Ltd., 3030 Cornwallis Road, Research Triangle Park, NC 27709 **On the importance of agonist concentration-gradients within isolated tissues. Increased maximal responses of rat vasa deferentia to (-)-noradrenaline after blockade of neuronal uptake.** Journal of Pharmacy and Pharmacology. 32(12):833-838, 1980.

The increased maximal responses of Sprague-Dawley rat vasa deferentia to (-)-noradrenaline (NA) after blockade of neuronal uptake by cocaine or desmethylimipramine were studied. Relationships between the neuronal uptake of NA, the free diffusion of NA into the tissue, and the number of smooth muscle cells required for production of maximal responses were examined. The data were compared with a theoretical calculation based on a model of restricted diffusion of enzyme substrates into structured tissues. The experimental data and theoretical calculations suggest that an altered concentration gradient of NA within the muscle layers is responsible for the increased maximal responses. Results indicate that an increase in maximal responses to agonists after blockade of uptake processes should not be taken as evidence of postsynaptic effects of the uptake inhibitor. 37 references. (Author abstract modified)

003880 Kerwin, R. W.; Olpe, H.- R.; Schmutz, M. Dept. of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **The effect of sodium-n-dipropyl acetate on gamma-aminobutyric acid-dependent inhibition in the rat cortex and substantia nigra in relation to its anticonvulsant activity.** British Journal of Pharmacology. 71(2):545-551, 1980.

Valproate sodium (100 to 400mg/kg i.p.) protected male SIV-50 rats from electroshock-induced convulsions, with the latency of the effect decreasing as a function of dose from 5 to 2 minutes. A parallel time course was seen for the inhibitory effect of valproate sodium (100 to 400mg/kg i.p.) on the spontaneous firing rate of cortical and nigral neurons. The inhibitory action of microiontophoretically applied GABA and muscimol on the firing rate of cortical neurons was potentiated within 1 to 3 minutes of microiontophoretic application of valproate sodium, but the inhibitory action of glycine was not affected. Microiontophoretically applied valproate sodium also potentiated inhibitory responses to GABA in rats pretreated with the GABA transaminase inhibitor gabaculine (100mg/kg i.p.). Valproate sodium did not markedly affect the duration of transsynaptic inhibitory responses recorded from the substantia nigra and cortex after submaximal electrical stimulation of the striatum and cortex, respectively. 24 references. (Author abstract modified)

003881 Kessler, John A.; Black, Ira B. Division of Developmental Neurology, Dept. of Neurology, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Nerve growth factor stimulates development of substance P in the embryonic spinal cord.** Brain Research. 208(1):135-145, 1981.

Development of the putative neurotransmitter substance-P (SP) was studied in vivo in the embryonic rat dorsal root ganglion (DRG) and spinal cord. SP was not detectable by radioimmunoassay before day 17 of gestation (E17). On E17, cervical sensory ganglia contained 4 pg SP/ganglion, rising to 49 pg/ganglion at birth. The dorsal cervical spinal cord contained 0.75 ng SP/mg protein on E17, rising to 6 ng SP/mg protein on postnatal day 3. The ventral spinal cord contained approximately 20% of the SP content in the dorsal spinal cord at each gestational age. Intrauterine forelimb amputation partially prevented the normal developmental increase of SP in sensory ganglia destined to innervate that limb, suggesting that target structures regulate the development of peptidergic neurons. Conversely, treatment with nerve growth factor (NGF) stimulated development of SP in the DRG. Moreover, NGF treatment increased SP in the dorsal spinal cord, suggesting that NGF can modulate development within the CNS, as well as in peripheral structures. It is likely that the CNS effect reflects NGF action on peripheral ganglia, but a direct effect on the spinal cord has not been excluded. However, treatment with antiserum to NGF failed to significantly inhibit development of ganglion SP. It is suggested that the system of SP containing neurons in the DRG may provide a convenient model for defining events regulating peptidergic maturation. 34 references. (Author abstract)

003882 Khachaturyan, G. S.; Kazaryan, K. A. NIL biosinteticheskikh reaktsiy mozga, Yerevanskiy meditsinskiy institut, Yerevan, USSR **/The effect of adenosine and guanosine on the content of serotonin and catecholamines in the brain in the restoration period following experimental clinical death./** Deystviye adenozina i guanozina na soderzhaniye serotonina i katekholaminov v mozge v vosstanovitel'nom periode posle eksperimental'noy klinicheskoy smerti. Zhurnal Eksperimental'noy i Klinicheskoy Meditsiny. 20(5):469-474, 1980.

The effect of adenosine and guanosine on the content of serotonin and catecholamines in the brain in the restoration period following experimental clinical death was studied in white male rats. Adenosine and guanosine were injected together with blood during revival of the organism. Results show that in the restoration period after revival of the organism, adenosine and guanosine stimulate the normalization of the level of serotonin, noradrenaline, and dopamine. Guanosine first has an effect on the normalization of the dopamine level, and then on the level of noradrenaline and serotonin. These results suggest that these nucleotides can be used in preventive treatment and therapy in terminal conditions. In addition, these results could be used as a basis for further study of the effect of nucleotides on the normalization of the content of serotonin, noradrenaline, and dopamine in the restoration period, as enzymes of their synthesis and breakdown. 15 references.

003883 Khanna, J. M.; Kalant, H.; Le, A. D.; Mayer, J.; LeBlanc, A. E. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **Effect of p-chlorophenylalanine on the acquisition of tolerance to the hypnotic effects of pentobarbital, barbital, and ethanol.** Canadian Journal of Physiology and Pharmacology. 58(9):1031-1041, 1980.

The effect of p-chlorophenylalanine (p-CPA on the acquisition of tolerance to the hypnotic effects of pentobarbital, barbital, and ethanol was investigated. Rats were given pentobarbital by daily intubation, and sleeping times and blood levels of drug were measured at awakening and after i.p. test doses of ethanol, pentobarbital, or barbital. No CNS tolerance to pentobarbital or cross-tolerance to barbital or ethanol occurred on treatment with sodium pentobarbital. However, when the size and frequency of pentobarbital treatment doses were increased from 50mg/kg/day to 50mg/kg to 80mg/kg thrice daily, a clear CNS tolerance to barbital occurred. Chronic administration of p-CPA, in a dose previously shown to maintain more than 95% depletion of brain serotonin (5-HT), enhanced the acute hypnotic effect of barbiturates and ethanol. Independently of this effect, p-CPA treatment also resulted in a reduction in development of CNS tolerance. Results are consistent with earlier findings that brain 5-HT depletion retards tolerance development to central depressant drugs as measured by a variety of unrelated tests. 41 references. (Author abstract modified)

003884 Khodorov, B. I.; Revenko, S. V. Biophysics Laboratory, Vishnevski Surgical Institute, Moscow, USSR **Further analysis of the mechanisms of action of batrachotoxin on the membrane of myelinated nerve.** Neuroscience. 4:1315-1330, 1979.

The mode of action of batrachotoxin on myelinated frog nerve fibers was investigated. Batrachotoxin altered a certain fraction of the sodium channels in the node of Ranvier frog so that the modified channels lost inactivation and opened and closed with exponential kinetics. Batrachotoxin shifted the sodium activation by 50 mV to more negative voltages and increased the maximum time constant of activation by factor of 10. Dose response relations for batrachotoxin-induced modification show that one batrachotoxin molecule modified one sodium channel, the dissociation constant being 1000 nM. The receptor for batrachotoxin in considered to be linked allosterically to all principle subunits of the sodium channel: the voltage sensor, the gates, and the selectivity filter. The similarity of the effects of batrachotoxin and anther potent alkaloid, aconitine, are pointed out. (Journal abstract modified)

003885 Kikvadze, I. N.; Ioseliani, T. K. Tbilisskiy gosudarstvennyy universitet, Tbilisi, USSR /**The effect of electrical stimulation of the locus coeruleus and intraperitoneal injection of certain pharmacological substances on the threshold of hippocampal afterdischarges.**/ Vliyaniye elektricheskogo razdrazheniya sinego pyatna i intraperitoneal'nogo vvedeniya nekotorykh farmakologicheskikh veshchestv na porog gippokampal'nykh razryadov posledeystviya. Soobshcheniya Akademii Nauk Gruzinskoy SSR. 100(1):193-196, 1980.

The effect of electrical stimulation of the locus coeruleus and the intraperitoneal injection of reserpine and L-DOPA on the threshold of hippocampal afterdischarges was studied in adult cats. Results show that: stimulation of the locus coeruleus significantly raised the threshold of hippocampal afterdischarges; reserpine (4mg/kg) lowered the threshold of epileptogenic stimulation, and diminished the inhibitory effect of the locus coeruleus stimulation, as well as the threshold of afterdischarges. 13 references. (Journal abstract modified)

003886 Klemm, William R. Dept. of Veterinary Anatomy, Texas A&M University, College Station, TX 77843 **Opiate mechanisms: evaluation of research involving neuronal action potentials.** Progress in Neuro-Psychopharmacology. 5(1):1-33, 1981.

Studies of the effects of opiates and opioids on unit activity are reviewed. Opiates generally depress neuronal activity with pharmacological stereospecificity, but excitatory effects occur in several brain regions, particularly during the development of tolerance. Opiates interact with major neurotransmitter systems in a variety of ways, but the mechanisms of these interactions are poorly understood. Opiates have profound effects in various brain structures associated with prominent behavioral effects of opiates, such as catalepsy, euphoria, reward, and analgesia. The widespread distribution of cells sensitive to both stereospecific and nonstereospecific effects of opiates suggests that the behavioral effects of opiates are mediated through several receptor types and several levels of the nervous system. 98 references. (Author abstract modified)

003887 Klugman, K. P.; Lembeck, F.; Markowitz, S.; Mitchell, G.; Rosendorff, C. Dept. of Physiology, University of the Witwatersrand Medical School, Hospital St., Johannesburg, South Africa **Substance P increases hypothalamic blood flow via an indirect adrenergic-cholinergic interaction.** British Journal of Pharmacology. 71(2):623-629, 1980.

Intrahypothalamic injections of 50 or 500mg substance-P increased hypothalamic blood flow (HBF) in conscious New Zealand rabbits. A 5ng dose of substance-P had no effect. The effect of substance-P was abolished by cholinoceptor blockade with atropine or mecamylamine and by adrenoceptor blockade with proproanolol or phenoxybenzamine. The vasodilator action of substance-P was also abolished by chemical sympathectomy of the hypothalamus with 6-hydroxydopamine or by destruction of the intracerebral nonadrenergic pathway (INP). Barbiturate and bicarbonate, which block the vasodilator action of the INP, also blocked the vasodilator effect of substance-P. Results suggest that substance-P may increase HBF via release of endogenous acetylcholine, which in turn stimulates the INP. 37 references. (Author abstract modified)

003888 Knych, E. T.; Eisenberg, R. M. Dept. of Pharmacology, University of Minnesota, School of Medicine, Duluth, MN 55812 **Effect of amphetamine on plasma corticosterone in the conscious rat.** Neuroendocrinology. 29:110-118, 1979.

The effect of amphetamine (AMPH) on plasma corticosterone was studied in the conscious, unstressed rat. AMPH (0.5 to 5.0mg/kg) produced a dose dependent increase in plasma corticosterone that was not altered by the adrenergic blocking agents phenoxybenzamine or propranolol. In contrast, the serotonergic depleting agent p-chloroamphetamine significantly inhibited the AMPH-induced rise in corticosterone. In addition, the serotonergic blocking agent methysergide, but not cyproheptadine, inhibited the corticosterone increase induced by AMPH. (Journal abstract)

003889 Kohler, Christer; Schwarcz, Robert. ASTRA Research Laboratories, ASTRA Lakemedel AB, Sodertalje, Sweden **Monosodium glutamate: increased neurotoxicity after removal of neuronal re-uptake sites.** Brain Research. 211(2):485-491, 1981.

Microinjections of monosodium glutamate (MSG) into the hippocampus of male Sprague-Dawley rats produced only marginal damage to local neurons. Hippocampal granule cells were markedly more vulnerable to the neurotoxic effect of MSG after perforant path transections, which removed their glutamatergic afferents. Results are discussed in relation to human neurodegenerative disorders such as Huntington's disease. 20 references. (Author abstract modified)

003890 Kohli, Jai D.; Goldberg, Leon I. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th St., Chicago, IL 60637 **Effects of 3',4'-dihydroxynomifensine on the dopamine vascular receptor.** Journal of Pharmacy and Pharmacology. 32(3):225-226, 1980.

The activity of 3',4'-dihydroxynomifensine as a dopamine (DA) vascular agonist was studied in the canine renal vascular bed. Results indicated that 3',4'-dihydroxynomifensine is a partial DA vascular agonist. The compound had weaker alpha-adrenergic effect than DA and showed no betal-adrenergic effects. Results suggest that further modification of the nomifensine molecule may yield a more potent DA agonist with relatively little effect on adrenergic receptors. 5 references.

003891 Krishnan, H.; Baquer, N. Z.; Singh, R/ Neurochemistry Unit, School of Life Sciences, Jawaharlal Nehru University, New Delhi-110 067, India **Changes in gamma-aminobutyric acid-shunt enzymes in regions of rat brain with ketamine anaesthesia.** Neuropharmacology. 20(6):567-574, 1981.

The effects of ketamine hydrochloride (100mg/kg i.p.) on the activity of glutamic acid decarboxylase (GAD), 4-aminobutyrate-2-oxoglutarate aminotransferase (GABA-T), and succinic semialdehyde dehydrogenase (SSA-DH) were studied in homogenates and subcellular fractions from female Wistar rat brainstem, cerebellum, and cerebral hemispheres. Ketamine increased GABA GAD activity in synaptosomal fractions from brainstem and cerebellum but not from the cerebral hemispheres. Ketamine inhibited GABA-T and SSA-DH activity (mitochondrial fractions) in brainstem, but caused only transient increases in

GABA-T and SSA-DH activity in cerebral hemispheres. In cerebellum (mitochrondrial fractions), ketamine had no effect on GABA-T activity, but inhibited SSA-DH activity. Results are discussed in relation to the anticonvulsant effect of ketamine. 30 references. (Author abstract modified)

003892 Kuhn, Donald M.; Wolf, William A.; Lovenberg, Walter. Section on Biochemical Pharmacology, Hypertension-Endocrine Branch, NHLBI, NIH, Building 10, Room 7N262, Bethesda, MD 20205 **Pressor effects of electrical stimulation of the dorsal and median raphe nuclei in anesthetized rats.** Journal of Pharmacology and Experimental Therapeutics. 214(2):403-409, 1980.

Electrical stimulation of the dorsal or median raphe nucleus in anesthetized rats produced a transient increase in arterial blood pressure. Heartrate and respiratory rate did not appear to change systematically after stimulation. Transections rostral or caudal to the raphe nuclei or electrolytic lesions in the area of the nucleus linearis, pars caudalis abolished the pressor response to stimulation. Depletion of brain serotonin with p-chloropheny-lalanine significantly attenuated the pressor effect of both dorsal and median raphe stimulation. The data suggest that stimulation of the ascending serotonergic neuronal system produces a phasic pressor effect which is mediated, at least in part, by synaptic serotonin. 23 references. (Author abstract modified)

003893 Kurosawa, Atsushi; Kageyama, Hiroyasu; John, Thoppil M.; Hirota, Ryoji; Itoh, Shinji. Shionogi Research Laboratory, Shionogi and Co., Ltd., Fukushima-ku, Osaka 553, Japan **Effect of neonatal hydrocortisone treatment on brain monoamines in developing rats.** Japanese Journal of Pharmacology. 30(2):213-220, 1980.

Subcutaneous injection of 0.5mg hydrocortison on postnatal day 2 significantly suppressed the development of whole brain in Wistar rats. Norepinephrine, dopamine, and serotonin contents in the brains of treated rats were higher than those in controls. Results suggested that hydrocortisone potentiated monoaminergic nervous systems in the hypothalamus, diencephalon, and pons/medulla oblongata. 26 references. (Author abstract modified)

003894 Laasberg, L. H.; Johnson, E. E.; Hedley-Whyte, J. Hedley-Whyte: 330 Brookline Avenue, Y-423, Boston, MA 02115 **Effect of morphine and naloxone on Leu-enkephalin-like immunoreactivity in dogs.** Journal of Pharmacology and Experimental Therapeutics. 212(3):496-502, 1980.

The effect of intravenously administered morphine sulfate and naloxone hydrochloride on leucine-enkephalin-like immunoreactivity (LELIR) in blood was determined. Is extracts of femoral artery and portal, jugular, and hepatic veins of 15 dogs anesthetized with pentobarbital, a compound with LELIR was present which cochromatographed on a thin layer plate with synthetic leucine-enkephalin and showed immunoreactivity with the antiserum to leucine-enkephalin bovine serum albumin complex. After morphine administration, the LELIR was approximately twice the control values, except in specimens from hepatic vein, where no apparent change was observed. Evidence supports the concept of multiple type receptors for receptor sites for endogenous opioid peptides and narcotic drugs. The catabolism of leucine-enkephalin-like material by the liver remains apparently unchanged during morphine and naloxone administration as judged from the enkephalin values in hepatic venous blood. 45 references. (Author abstract modified)

003895 Laborit, G.; Baron, C.; Topal, G.; Henriet, I. Hopital Boucicaut, 78, rue de la Convention, F-75730 Paris Cedex 15, France **/Na gamma hydroxybutyrate in cerebral protection during severe hypoxemia in the rat./** Interet du gamma hydroxybutyrate de Na dans la protection cerebrale au cours des hypoxies severes chez le rat. Agressologie. 21(4):189-197, 1980.

The effect of 4-sodium hydroxybutyrate (4-OHB) on induced anoxias in rats was studied. Anoxia was induced in two groups of rats, with and without the protection of either 4-OHB or pentobarbital. In the first group, pH and plasmatic lactate were measured before and after anoxia while cerebral elctrogenesis was controlled; in the second group, levels of norepinephrine, dopamine, 5-HT, and lactic acid in brain tissue were measured. Results show that plasmatic pH before anoxia is unchanged with 4-OHB and lowered with pentobarbital; immediately after anoxia plasmatic pH is lowered less by 4-OHB than by pentobarbital. In brain tissue 4-OHB raises the level of norepinephrine significantly, whereas pentobarbital does not. Similar results were found with dopamine. Concentrations of 5-HT varied little, and levels of lactic acid were increased most by pentobarbital. The increase in norepinephrine and dopamine with 4-OHB explains the favorable results with humans when using this substance to protect the brain. 38 references. (Journal abstract modified)

003896 Laduron, P. M.; Leysen, J. E.; Gorissen, H. Dept. of Biochemical Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Muscarinic receptor: multiple sites or unitary concept?** Archives Internationales de Pharmacodynamie et de Therapie. 249(2):319-321, 1981.

The binding of 3H-dexetimide was studied in various brain regions of rats and dogs and in dog stomach. The potency of pirenzepine in displacing 3H-dexetimide was similar in striatum, cortex, and stomach. The potency of atropine was also similar in the various preparations studied. These findings do not support the suggestion that there are multiple sites or subclasses of muscarinic acetycholine receptors. 6 references.

003897 Larsson, P. A.; Dahlstrom, A.; Heiwall, P. O.; Booj, S. Institute of Neurobiology, University of Goteborg, Goteborg, Sweden **The effect of chronic nicotine and withdrawal on intraaxonal transport of acetylcholine and related enzymes in sciatic nerve of the rat.** Journal of Neural Transmission. 47:243-251, 1980.

The content of acetylcholine (ACh) and activities of the cholinergic enzymes choline acetyltransferase (CAT) and ACh-esterase (AChE) were studied in intact and crushed rat sciatic nerve after chronic nicotine administration and withdrawal 2 days before the final experiment. Nicotine was given in the drinking water during 8 to 10 weeks and the final dose reached was about 8mg/kg/day, i.e., equivalent to that of the heavy cigarette smoker. In the chronic nicotine group, ACh levels and AChE activity of uncrushed nerve were significantly decreased as compared to the controls. The accumulation of ACh and AChE proximal to a single crush was also somewhat decreased, but significant only for AChE at 18 hours postoperatively. After withdrawal of nicotine for 2 days, the ACh content of both uncrushed and 12 hours crushed nerves were further decreased, while AChE was instead increased to control (uncrushed) or even supranormal (18 hour crush) levels. (Journal abstract)

003898 Le Fur, G.; Mizoule, J.; Burgevin, M. C.; Ferris, O.; Heaulme, M.; Gauthier, A.; Gueremy, C.; Uzan, A. Pharmindustrie, Groupe PHARMUKA, 35, Quai du Moulin de Cage, F-92231 Gennevilliers, France **Multiple benzodiazepine receptors: evidence of a dissociation between anticonflict and anticonvulsant properties by PK 8165 and PK 9084 (two quinoline derivatives).** Life Sciences. 28(13):1439-1448, 1981.

Evidence of a dissociation between the anticonflict and anticonvulsant properties of two quinoline derivatives (PK-8165 and

PK-9084) is presented. These drugs appeared to be more potent at displacing (3H)diazepam from its binding sites in the presence of halides suggesting that they are acting on benzodiazepine receptors associated to a chloride ionophore. Like the benzodiazepines, PK-8165 and PK-9084 increase punished responding in the rat conflict procedure but do not produce ataxia or sedation even at doses five to 20 times higher than those which are effective in the conflict test. Moreover, they do not possess anticonvulsant properties. PK-8165 and PK-9084 do not change cyclic GMP content of the cerebellar cortex and do not antagonize the increase in cyclic GMP induced by the GABA antagonists isoniazid and picrotoxin. Thus PK-8165 and PK-9084 pure anticonflict drugs might act on GABA independent benzodiazepine receptors associated to a chloride ionophore. 33 references. (Author abstract modified)

003899 Le Fur, Gerard; Guilloux, Francoise; Kabouche, Marie; Mitrani, Nicole; Ferris, Odette; Uzan, Andre. Uzan: Pharmindustrie, Groupe PHARMUKA, 35, quai du Moulin de Cage, F-92231 Gennevilliers, France **Central dopaminergic neurons during development of genetic and DOCA-salt hypertension in the rat.** Developmental Brain Research. 1(2):153-163, 1981.

The in vivo binding of (3H)spiroperidol was measured in discrete areas of the brain in 7-week-old, 9-week-old, and 16-week-old spontaneously hypertensive rats (SHR) and age matched normotensive Wistar-Kyoto (WKY) controls. An increase in the (3H)spiroperidol binding in the striatum, tuberculum olfactorium, and frontal cortex but not in the cerebellum was detected at all ages in SHR. The increase was more pronounced in 7-week-old SHR than in 9-week-old or 16-week-old SHR rats. In vitro data indicate an increase in Bmax but no variation in Kd in the striatum of 7-week-old SHR. The DOPA accumulation after injection of the DOPA decarboxylase inhibitor NSD 1015 was greater in the tuberculum olfactorium from 7-week-old SHR. An increase in (3H)spiroperidol binding sites was also observed in the striatum and tuberculum olfactorium after 7 weeks of deoxycorticosterone (DOCA) salt treatment. Results suggest that dopaminergic neurons might be implicated in that onset of hypertension in the rat. 31 references. (Author abstract modified)

003900 Lee, Chi Ho; Strosberg, Arthur M.; Warren, Lea Ann. Dept. of Pharmacology, Syntex Research, Palo Alto, CA 94304 **The importance of catecholamine uptake inhibition in the reversal of guanethidine blockade of adrenergic neurons.** Research Communications in Chemical Pathology and Pharmacology. 30(1):3-14, 1980.

Desipramine, imipramine, viloxazine, tripelennamine, tranylcypromine, and d-amphetamine reversed the adrenergic blocking activity of guanethidine against pressor responses induced by spinal electrical stimulation in pithed male Sprague-Dawley rats. Although these compounds are from different pharmacological classes, all have neuronal uptake inhibitory activity. It is suggested that inhibition of catecholamine uptake is sufficient to antagonize guanethidine adrenergic neuron blockade. 22 references. (Author abstract modified)

003901 Leelavathi, Doddamane E.; Misra, Chandra H.; Shelat, Harnath; Smith, Robert C. Smith: Texas Research Institute of Mental Sciences, 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Effects of acute and chronic administration of phencyclidine on dopaminergic receptors in rat striatum.** Communications in Psychopharmacology. 4(5):417-424, 1980.

The effects of acute and chronic administraton of phencyclidine (PCP) on dopaminergic receptors in rat striatum are discussed. PCP (10mg/kg) produced a significant decrease in dopamine (DA) stimulated adenylate cyclase activity and phosphodiesterase activity in rat striatum, both after a single PCP dose and 24 hours after 30 days of chronic PCP injections. However, 15 minutes after the 31st PCP dose, there was a relative increase in striatal DA stimulated adenylate cyclase activity compared to chronic PCP rats who received saline on day 31. PCP added in vitro did not displace specific 3H-spiperone binding to rat striatal membranes, but PCP 10mg/kg injected into rats produced a small but significant increase in specific binding of spiperone in rat striatum. 23 references. (Author abstract modified)

003902 Leslie, Frances M.; Chavkin, Charles; Cox, Brian M. Cox: Addiction Research Foundation, 701 Welch Road, Palo Alto, CA 94304 **Opioid binding properties of brain and peripheral tissues: evidence for heterogeneity in opioid ligand binding sites.** Journal of Pharmacology of Experimental Therapeutics. 214(2):395-402, 1980.

The specific binding of (3H)dihydromorphine ((3H)DHM) and (3H)D-Ala2-D-Leu5-enkephalin ((3H)DADLE) to binding sites in bovine corpus striatum, bovine adrenal medulla, guinea-pig, rabbit, and rat ileum, and mouse vas deferens has been characterized. In all tissues, the properties of high affinity (3H)DADLE binding sites were discriminable from (3H)DHM binding sites in terms of the relative potencies of competing opioid ligand. (3H)DADLE binding was more readily displaced by peptide opioids such as D-Ala2-L-Leu5-enkephalin than by alkaloids such as morphine, whereas (3H)DHM sites showed the reverse selectivity. Correlation of relative ligand potencies indicate that the enkephalin selective or alkaloid selective binding sites display similar properties across tissues and species. 33 references. (Author abstract modified)

003903 Leung, Lai-Wo Stan. Dept. of Psychology, University of Western Ontario, London, Ontario N6A 5C2, Canada **Differential effects of pentobarbital and ether on the synaptic transmission of the hippocampal CA1 region in the rat.** Electroencephalography and Clinical Neurophysiology. 51(3):291-305, 1981.

The effect of ether and sodium pentobarbital on the synaptic transmission of the hippocampal CA1 region was studied in chronically implanted rats. Animal behavior, EEG, and average evoked potentials (AEPs) following electrical stimulation of the alveus or the striatum radiatum of the CA1 region were recorded. Components of the AEPs, interpreted previously as generated by population excitatory postsynaptic potentials (EPSPs), population inhibitory postsynaptic potentials (IPSPs) or population postsynaptic spikes were differentially sensitive to ether or pentobarbital. It is concluded that ether and pentobarbital both suppress hippocampal neuronal excitability but the effect of anesthesia differs for different anesthetics, for different synapses, and for different levels of activity in the input fibers. 37 references. (Author abstract modified)

003904 Levin, Barry E. Veterans Administration Medical Center, East Orange, NJ 07019 **Reserpine effect on the axonal transport of dopamine-beta-hydroxylase and tyrosine hydroxylase in rat brain.** Experimental Neurology. 72(1):99-112, 1981.

Th effects of reserpine on the axonal transport of dopamine-beta-hydroxylase (DBH) and tyrosine hydroxylase (TH) were investigated in rats with 6-hydroxydopamine (6-OHDA) lesions in the rostral forebrain. Both BDH and TH activities accumulated linearly for 48 hours in the anterior hypothalamic sections proximal to the lesions. While DBH activity decreased toward baseline over the next 4 days, TH activity remained at the 48 hour levels, suggesting a faster turnover time of DBH activity at the lesion site. Accumulation of both enzymes was totally blocked by ipsilateral 6-OHDA lesions in the ascending dorsal and ventral noradrenergic bundles, suggesting that dopaminergic fibers do not contribute significantly to the accumulation of

TH activity. Reserpine induced DBH and TH production in noradrenergic neurons of the locus coeruleus was followed, after a delay of days, by increased levels in distally innervated regions. Single dose reserpine administration produced transient and sporadic decreases in the axonal transport of DBH and TH during the first 5 days after injection, followed by a steady increase to 693% of control for DBH at 7 days and 270% at 8 days for TH. This delay is attributed to delay in the onset of increased enzyme transport from the cell bodies. 46 references. (Author abstract modified)

003905 Levin, Barry E.; Comai, Karen; Sullivan, Ann C. Neurology Service (127), V.A. Medical Center, East Orange, NJ 07019 **Metabolic and sympatho-adrenal abnormalities in the obese Zucker rat: effect of chronic phenoxybenzamine treatment.** Pharmacology Biochemistry and Behavior. 14(4):517-525, 1981.

Male homozygous lean and obese Zucker rats were subjected to various stresses that activate the sympathoadrenal system and to chronic treatment with the alpha-adrenergic receptor blocker phenoxybenzamine (PBZ, 16 to 19 days). The obese Zucker rat exhibited abnormalities of lipid and carbohydrate metabolism that were corrected (hyperinsulinemia), induced (hyperglycemia), or exaggerated (hyperglycerolemia) by stress-induced activation of the sympathoadrenal systems. Chronic PBZ treatment increased baseline sympathetic activity in the obese rat and led to marked improvement in hyperinsulinemia. Weight loss was associated with a significant decrease in food intake in lean rats, but not in obese rats. Results suggest that a sympathoadrenal dysfunction may account for some of the metabolic abnormalities seen in obese Zucker rats. 53 references. (Author abstract modified)

003906 Lin, Chun Wel; Maayani, Saul; Wilk, Sherwin. Wilk: Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, One Gustave Levy Place, New York, NY 10029 **The effect of typical and atypical neuroleptics on binding of (3H)spiroperidol in calf caudate.** Journal of Pharmacology and Experimental Therapeutics. 212(3):462-468, 1980.

The effect of typical and atypical neuroleptics on the binding of (3H)spiroperidol to calf caudate membranes was studied. Saturable or specific binding was defined as the difference between binding in the absence and in the presence of 1mcM d-butaclamol. The inhibition constants (Ki) and IC50 values for various typical and atypical neuroleptics and for two clinically inactive butyrophenones were determined. The Ki and IC50 values of typical neuroleptics paralleled their potencies in vivo. In contrast, the binding potencies of atypical neuroleptics did not correlate with their effects in vivo. The most striking discrepancy between binding and properties in vivo was found for the benzamide derivatives, sulpiride and metoclopramide. It is concluded that binding assays with (3H)spiroperidol in calf caudate cannot account for the antidopamine effects in vivo of atypical neuroleptics. 46 references. (Author abstract modified)

003907 Lin, M. T.; Chandra, A.; Liu, G. G. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan **The effects of theophylline and caffeine on thermoregulatory functions of rats at different ambient temperatures.** Journal of Pharmacy and Pharmacology. 32(3):204-208, 1980.

Central and systemic administration of theophylline and caffeine produced dose dependent increases in rectal temperature in male Sprague Dawley rats in ambient temperatures of 8, 22, and 30 degrees C. The xanthines also produced behavioral excitation, cutaneous vasodilation, and diuresis. Respiratory evaporative heat loss was not altered, but metabolic heat production was increased. The xanthine-induced hyperthermia was antagonized by destruction of central catecholaminergic nerve fibers with 6-hydroxydopamine and by blockade of alpha-adrenergic and dopaminergic receptors with phentolamine and haloperidol. Results suggest that theophylline and caffeine elicit central activation of adrenergic and dopaminergic receptors via release of endogenous catecholamines. 24 references. (Author abstract modified)

003908 Lindamood, Charles, III; Colasanti, Brenda K. Dept. of Pharmacology and Toxicology, West Virginia University Medical Center, Morgantown, WV 26506 **Effects of delta9-tetrahydrocannabinol and cannabidiol on sodium-dependent high affinity choline uptake in the rat hippocampus.** Journal of Pharmacology and Experimental Therapeutics. 213(2):216-221, 1980.

Dose of delta9-tetrahydrocannabinol (delta9-THC) and cannabidiol (CBD) affording the same degree of protection against seizures induced by maximal electroshock were compared for their effects on sodium dependent high affinity choline uptake into six rat brain regions (cortex, striatum, medulla/pons, hypothalamus, midbrain, and hippocampus). One hour after administration of CBD, choline uptake was not altered in any brain region. In contrast, 1 hour after adminsitration of delta9-THC, choline uptake in hippocampus and hypothalamus was significantly reduced. Moreover, in vivo administration of delta9-THC was followed by a dose related reduction in vitro hippocampal choline uptake. After direct addition to the hippocampal homogenates, both delta9-THC and CBD inhibited choline uptake. Results suggest that the septal/hippocampal cholinergic tract is a major site of action of delta9-THC and may provide a neurochemical basis for the differntial pharmacological properties of delta9-THC and CBD. 30 references. (Author abstract modified)

003909 Lindberg, Iris; Dahl, June L. Dahl: Dept. of Pharmacology, University of Wisconsin Medical School, 426 N. Charter St., Madison, WI 53706 **Characterization of enkephalin release from rat striatum.** Journal of Neurochemistry. 36(2):506-512, 1981.

Antisera specific for methionine-enkephalin and leucine-enkephalin were used to study the release of these peptides from male Holtzmann rat striatal slices. Only 2 to 3% of the total tissue stores of enkephalin could be released by potassium depolarization. Similar percentages were released from globus pallidus, thalamus, and nucleus accumbens. No enkephalin release from hippocampus was detected. Striatal release of enkephalins was altered by changes in potassium and calcium levels in the superfusion medium, but lithium had no effect on basal or potassium stimulated release. Striatal enkephalins were stable during the short-term incubation periods used in these experiments. 29 references. (Author abstract modified)

003910 Lindvall, Olle; Ingvar, Martin; Stenevi, Ulf. Laboratory of Experimental Brain Research, University of Lund, Lund, Sweden **Effects of metamphetamine on blood flow in the caudate-putamen after lesions of the nigrostriatal dopaminergic bundle in the rat.** Brain Research. 211(1):211-216, 1981.

Metamphetamine was given to male Wistar rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal dopaminergic bundle. Local cerebral blood flow, measured autoradiographically with (14C)iodoantipyrine as the diffusible tracer, was more than twice as high in the denervated caudate/putamen than in controls. Measurements of local glucose consumption with the (14C)deoxyglucose technique showed no corresponding change in local metabolic rate; in fact, glucose consumption was reduced in the caudate/putamen on the lesioned side. Results indicate that the amphetamine-induced increase in cerebral blood flow does not require an intact nigrostriatal dopaminergic system. Dopamine relased by amphetamine appeared to constrict the vessels and reduce blood flow in the caudate putamen. 20 references. (Author abstract modified)

003911 Listinsky, Jay J.; Kohli, Jai D.; Goldberg, Leon I. Kohli: Dept. of Pharmacology, University of Chicago, 947 East 58th St., Chicago, IL 60637 **Consistent unmasking of dopamine-induced dilation of the canine femoral vascular bed.** Journal of Pharmacology and Experimental Therapeutics. 215(3):662-667, 1980.

Dopamine (DA) produced dose related vasodilation in the canine femoral vascular bed after the administration of two alpha-adrenergic blocking agents, WR-149,024 or yohimbine. DA-induced vasodilation unmasked by yohimbine was not antagonized by propranolol, pyrilamine, and metiamide, hexamethonium, or atropine, but was attenuated selectively by the DA antagonist sulpiride. The R-enantiomer of sulpiride was more effective than the S-enantiomer in attenuating DA-induced dilation. Phenoxybenzamine produced moderate (apparently nonspecific) attenuation of vasodilator responses to DA. The weaker vascular DA agonist, N,N-di-n-propyl dopamine, was approximately 4% the potentcy of DA in eliciting femoral vasodilation after yohimbine treatment. These findings suggest that DA produces femoral vasodilation after WR-149,024 or yohimbine by activation of vascular DA receptors similar to those proposed to exist in the renal vascular bed. 30 references. (Author abstract modified)

003912 Loomis, Christopher W.; Racz, William J. Dept. of Pharmacology, Queen's University, Kingston, Ontario, Canada K7L 3N6 **Drug interactions of amitriptyline and nortriptyline with warfarin in the rat.** Research Communications in Chemical Pathology and Pharmacology. 30(1):41-58, 1980.

The interaction of tricyclic antidepressants with warfarin and their effects on hepatic drug metabolism were studied in male Sprague-Dawley rats. Treatment with amitriptyline or nortriptyline for 6 days (6, 15, or 30mg/kg i.p.) did not increase the activities of aniline hydroxylase and did not alter the content of microsomal protein. Significant decreases in aminopyrine N-demethylase activity and cytochrome P-450 content were observed with the 30mg/kg dose. Amitriptyline and nortriptyline increased the prothrombin time of warfarin treated rats. At high tricyclic antidepressant doses, these increases in prothrombin time correlated with increases in the plasma half-life of warfarin. In vitro studies suggested that amitriptyline and nortriptyline competitively inhibited the metabolism of warfarin. The inhibition of warfarin metabolism and enhanced anticoagulant effect were greater after nortriptyline than after comparable doses of amitripyline. 27 references. (Author abstract modified)

003913 Loonen, Anton J. M.; Soe-Agnie, Carmen J.; Soudijn, Willem. Psychiatric Hospital Voorburg, P.O. Box 10150, 5260 GB Vught, The Netherlands **Effects of halopemide on GABA receptor binding, uptake and release.** Brain Research. 210(1-2):485-492, 1981.

The effects of halopemide on GABA uptake, receptor binding, and release were studied in male Wistar rat forebrain preparations in vitro. Results indicated that halopemide and its putative metabolites may interfere with GABA related synaptic mechanisms. The antipsychotic agent was similar to related neuroleptics in its effect on GABA uptake, release, and receptor binding. It is suggested that antagonistic effects of halopemide metabolites may contribute to its antipsychotic actions and lack of extrapyramidal side-effects. 19 references.

003914 Loscher, W. Free University of Berlin, School of Veterinary Medicine, Koserstrasse 20, D-1000 Berlin 33, West Germany **Effect of inhibitors of GABA aminotransferase on the metabolism of GABA in brain tissue and synaptosomal fractions.** Journal of Neurochemistry. 36(4):1521-1527, 1981.

The effects of five inhibitors of the GABA degrading enzyme GABA aminotransferase (GABA-T) (gabaculine, gamma-acetylenic GABA, gamma-vinyl GABA, ethanolamine O-sulphate, and aminooxyacetic acid), GABA, and the antiepileptic sodium valproate on the metabolism of GABA in brain tissue and synaptosomal fractions were investigated. The experimental mice were killed at the time of maximal anticonvulsant effect of the respective drugs and GABA, GABA-T, and glutamate decarboxylase (GAD) were determined in whole brain and synaptosomes. All drugs studied brought about significant increases in both whole brain and synaptosomal GABA concentrations, and, except GABA itself, inhibited the activity of GABA-T. Furthermore, all drugs, except GABA and gamma-acetylenic GABA, activated GAD in the synaptosomal fraction. Results suggest that activation of GAD is an important factor in the mechanism by which several inhibitors of GABA-T and also valproate increase GABA concentrations in nerve terminals, at least in the relatively nontoxic doses employed. 30 references. (Author abstract modified)

003915 Lucot, James B.; McMillan, D. E.; Leander, J. David. McMillan: University of Arkansas for Medical Sciences, 4301 West Markham Street, Little Rock, AR 72201 **The behavioral effects of d-amphetamine alone and in combination with acute and chronic morphine treatments in rats.** Journal of Pharmacology and Experimental Therapeutics. 210(2):158-165, 1979.

The behavioral effects of d-amphetamine were determined in rats responding under fixed-interval 5 minute or multiple fixed-interval 2.5 minute fixed-ration 30 response schedule of food presentation. The behavioral effects of d-amphetamine then were redetermined either in combination with acute doses of morphine or when the rats were drinking a .5 or a 1 mg/ml morphine solution, when the rats were undergoing withdrawal from morphine, and after withdrawal from morphine was presumed complete. Across the different control rates of responding, morphine and d-amphetamine administered alone produced dose related decreases in responding. The combination of d-amphetamine with acute doses of morphine produced effects which were greater than the sum of the effects of each drug alone. The daily dose of orally consumed morphine increased throughout the morphine drinking period. The rats displayed gross signs of withdrawal, particularly large losses in bodyweight (but not disruption of operant responding), when the morphine solution was withheld for 24 hours before a session. The effects of d-amphetamine were not altered during morphine drinking, during morphine withdrawal, or after withdrawal was presumed complete. 32 references. (Author abstract)

003916 Lullmann-Rauch, R.; Thesleff, S. Dept. of Anatomy, University of Kiel, Kiel, West Germany **Effects of taipoxin on the ultrastructure of cholinergic axon terminals in the mouse adrenal medulla.** Neuroscience. 4:837-841, 1979.

The effects of intravenous injections of the neurotoxin, taipoxin, on the ultrastructure of cholinergic axon terminals were investigated in the mouse adrenal medulla. Conspicuous changes were found in the ultrastructure of axon terminals upon chromaffin cells in the adrenal gland. The alterations were in several respects similar to those previously described at the neuromuscular junction. The electron density of the axoplasm was greatly increased and the mitochondria swollen. In many instances the number of synaptic vesicles was reduced. The alterations were more marked the longer the period of toxin action. It is suggested that the toxin molecule, which has phospholipase A2 activity, enters the axoplasm before exerting a hydrolytic and thereby neurotoxic action on cholinergic nerve terminals. (Journal abstract modified)

003917 Lundberg, Dag B. A.; Mueller, Robert A.; Breese, George R. Mueller: Dept. of Anesthesiology, School of Medicine, University of North Carolina, NCMH 204H, Chapel Hill, NC 27514 **An evaluation of the mechanism by which serotonergic activation depresses respiration.** Journal of Pharmacology and Experimental Therapeutics. 212(3):397-404, 1980.

The central or peripheral mechanism by which serotonergic activation depresses respiration was explored. Systemic administration of 5-hydroxytryptophan (5-HTP) to pargyline treated animals and 5-methoxy-N,N-di-methyltryptophan (5-MDMT) probably depress respiration secondary to central penetration of these drugs, since: 1) adult rats with biochemical evidence of partial destruction of central serotonergic neurons after neonatal intracisternal 5,7-dihydroxytryptamine were supersensitive to the respiratory depressing effect of 5-HTP and 5-MDMT; 2) the ventilatory effect of the serotonergic agonists was not reduced by surgical deafferentiation induced by bilateral transection of the glossopharyngeal nerves; 3) after sectioning of the vagus nerve, the absolute change produced by serotonergic agonists was less; and 4) inhibition of peripheral aromatic amino acid decarboxylase by RO-4-4602 significantly blunted the respiratory depressant activity of 5-HTP observed at 15 minutes, but not that present 30 minutes after 5-HTP. Results suggest that the central nervous system areas involved in respiratory control may be modulated at some level by the activity of central serotonergic neurons. 30 references. (Author abstract modified)

003918 Lynch, Gary S.; Jensen, Robert A.; McGaugh, James L.; Davila, Kenneth; Oliver, Michael W. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Effects of enkephalin, morphine, and naloxone on the electrical activity of the in vitro hippocampal slice preparation.** Experimental Neurology. 71(3):527-540, 1981.

The effects of infusion of low concentrations of D-Ala-D-Leu-enkephalin, morphine, or naloxone on electrical responses to stimulation of the in vitro hippocampal slice preparation were investigated. Concentrations of enkephalin as low as 10 nM and morphine as low as 1 mcM dramatically increased the magnitude of the population spike response of pyramidal cells to Schaffer commissural stimulation. Enhancement of the population spike by either morphine or enkephalin was blocked by the opiate receptor antagonist naloxone. The response to antidromic stimulation was not altered by enkephalin, nor was the slope of the dendritic response, indicating that the enkephalin effect is not mediated by depolarization of the pyramidal cells themselves nor by facilitation of synaptic processes at the dendrites. The possibility that the enkephalin effect might be produced by alteration of either a feed forward or a feedback mechanism mediated by basket cells was investigated. It is suggested that enkephalin acts to alter the efficiency of a mechanisms involved in coupling the dendritic excitatory postsynaptic potential with the spike initiation mechanisms of the cell body. 18 references. (Author abstract modified)

003919 Machula, A. I.; Barkov, N. K.; Pokryshkin, V. I. Barkov: Laboratoiya, Tsentral'nyy NII sudebnoy psikhiatrii im. prof. Serbskogo, MZ SSSR, Moskva, USSR **/The effect of psychostimulants on changes in the excitability of the visual cerebral cortex./** Osobennosti izmeneniy vozbudimosti zritel'noy oblasti kory golovnogo mozga pri deystvii psikhostimulyatorov. Farmakologiya i Toksikologiya. 43(4):338-341, 1980.

The effect of psychostimulants on changes in the excitability of the visual cerebral cortex was studied in cats by recording the primary responses of the visual cortex with the aid of implanted electrodes. Results show that amphetamine (0.5mg/kg), sydnocarb (3mg/kg), and catinon (1mg/kg) depressed the primary response amplitude and concurrently lessened the depression of the testing response in the primary response recovery cycle. Results also show that cocaine (1mg/kg) suppressed the amplitude of the primary responses and intensified the depression of the testing primary response in the recovery cycle. 4 references. (Journal abstract modified)

003920 Maeda, Kiyoshi; Frohman, Lawrence A. Frohman: Division of Endocrinology and Metabolism, Michael Reese Medical Center, 2900 S. Ellis Ave., Chicago, IL 60616 **Neurotensin release by rat hypothalamic fragments in vitro.** Brain Research. 210(1-2):261-269, 1981.

The release of neurotensin by male Sprague-Dawley rat hypothalamic fragments in vitro was studied. Neurotensin-like immunoreactivity released into the incubation medium coeluted with synthetic neurotensin on gel filtration chromatography and paralleled synthetic neurotensin in radioimmunoassay. Neurotensin-like immunoreactivity released into the incubation medium was degraded by released hypothalamic peptidases, and this degradation was partially prevented by bacitracin. Neurotensin release was stimulated by dibutyryl cyclic AMP and by depolarizing concentrations of potassium; the latter effect was calcium dependent. Dopamine stimulated neurotensin release in a dose dependent manner, and this effect was blocked by haloperidol. Neurotensin release was not stimulated by norepinephrine or serotonin. 20 references. (Author abstract modified)

003921 Maitre, L.; Moser, P.; Baumann, P. A.; Waldmeier, P. C. no address **Amine uptake inhibitors: criteria of selectivity.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):97-110, 1980.

The effects of classical antidepressants and newer, potentially antidepressant drugs on the uptake of noradrenaline (NA) and serotonin (5-HT) were measured in a number of in vivo and in vitro test systems and the correlations between the results obtained in the different test systems were calculated. Good correlations were found between the prevention of amine depletion induced by H77/77 or H75/12 and the effects on amine uptake in synaptosomal preparations from treated animals. For between systems measuring peripheral and central amine uptake inhibition the correlations were less clear, but still significant. Those between in vitro and in vivo test systems were generally very poor. It is suggested that in estimating the selectivity of amine uptake inhibitors, a procedure measuring central amine uptake in vivo should be chosen and only data relating on one single system should be compared. 23 references.

003922 Mandell, Arnold J.; Bullard, Wilson P.; Yellin, Joseph B.; Russo, Patrick V. Dept. of Psychiatry, University of California, La Jolla, CA **The influence of d-amphetamine on rat brain striatal reduced biopterin concentration.** Journal of Pharmacology and Experimental Therapeutics. 213(3):569-574, 1980.

The effects of d-amphetamine on levels of reduced biopterin (BH4) in male Sprague-Dawley rat striatum were examined. In untreated rats, striatal BH4 levels varied diurnally by twofold, oscillating around a concentration of 3mcM. D-amphetamine consistently induced a decrease in BH4 levels that did not exceed 25 to 30%. Recovery of control levels required several hours. Several other psychotropic drugs, including other stimulants and phenylethylamine congeners, failed to induce a similar change in BH4 level. The amphetamine effect was blocked by methylphenidate and reserpine. The prolonged time for BH4 recovery may have been due to an amphetamine-induced functional uncoupling of quinonoid dihydropteridine reductase from striatal tyrosine hydroxylase, leading to spontaneous isomerization of the partially reduced pterin to its nonquinonoid form, which is not a substrate for the BH4 regenerating enzyme. 43 references. (Author abstract modified)

003923 Mangano, Richard M.; Schwarcz, Robert. Schwarcz: Maryland Psychiatric Research Center, P.O. Box 3235, Baltimore, MD 21229 **The human platelet as a model for the glutamatergic neuron: platelet uptake of L-glutamate.** Journal of Neurochemistry. 36(3):1067-1076, 1981.

The kinetic and pharmacological properties of glutamate uptake mechanisms in human platelets and rat brain crude synaptosomal preparations were compared. A sodium dependent high affinity L-glutamate uptake system and a temperature dependent low affinity uptake site were demonstrated in human platelets. Kinetic properties were similar to those in rat brain synaptosomes, but maximal velocity values were higher in rat brain. Threo-3-hydroxy-DL-aspartate, DL-aspartate-beta-hydroxamate, L-glutamate, and L-aspartate had similar effects in the human platelet and rat brain synaptosome preparations. Studies of intrasubject and intersubject variability in human volunteers indicate that glutamate uptake measurements in human platelets are suitable for clinical studies. 34 references. (Author abstract modified)

003924 Marchbanks, R. M.; Wonnacott, S.; Rubio, M. A. Dept. of Biochemistry, Institute of Psychiatry, London SE5 8AF, England **The effect of acetylcholine release on choline fluxes in isolated synaptic terminals.** Journal of Neurochemistry. 36(2):379-393, 1981.

Choline influx into guinea-pig cortical synaptosomes was enhanced after a period of depolarization-induced release of acetylcholine (ACh). Influx was stimulated by high internal concentrations of choline, and efflux was stimulated by high external concentrations. The maximal influx and efilux at saturating opposite concentrations of choline were equal, with a value of 500pmol/minute/mg synaptosomal protein. Increased ACh concentrations inhibited choline influx and efflux from the trans position. Increased intrasynaptosomal ACh concentrations abolished the stimulation of influx by depolarization. It is suggested that high concentrations of ACh immobilize the choline carrier on the inside of the synaptic membrane and that ACh release relieves this immobilization. 38 references. (Author abstract modified)

003925 Marin, J.; Sanchez, C. F. Depto. de Farmacologia y Terapeutica, Facultad de Medicina, Universidad Autonoma, C/ Arzobipo Morcillo, 1, Madrid 34, Spain **Influence of calcium on noradrenaline release evoked by 5-hydroxytryptamine, tyramine and potassium from goat pial arteries.** Journal of Pharmacy and Pharmacology. 32(9):643-646, 1980.

The release of tritium evoked by tyramine, potassium (K), and 5-hydroxytryptamine (5-HT) from goat pial arteries preloaded with tritiated noradrenaline (NA) was studied. In normal Krebs-bicarbonate solution, all three agents caused a transient increase in radioactivity release. The effects of tyramine and 5-HT had slow onset and decline, but K produced a rapid peak of 3H release followed by a quick decline. Removal of calcium ions (Ca2) from the medium did not alter the effect of tyramine, markedly reduced the effect of K, and partially reduced the afflux evoked by 5-HT. Results indicate that K evokes NA release from brain vessels by a Ca2 dependent process, probably of an exocytotic nature, whereas tyramine mediates NA release via a Ca2 independent mechanism. The 5-HT effect appears to involve both components. 16 references. (Author abstract modified)

003926 Marwaha, Jwaharlal; Palmer, Michael R.; Woodward, Donald J.; Hoffer, Barry J.; Freedman, Robert. Freedman: Dept. of Psychiatry, C268, University of Colorado Health Sciences Center, 4200 E. Ninth Avenue, Denver, CO 80262 **Electrophysiological evidence for presynaptic actions of phencyclidine on noradrenergic transmission in rat cerebellum.** Journal of Pharmacology and Experimental Therapeutics. 215(3):606-613, 1980.

The actions of the psychotomimetic drug phencyclidine (PCP) were studied using Purkinje neurons in the cerebellum of urethane anesthetized rats. PCP, applied by micropressure ejection through multibarreled micropipettes, depressed the spontaneous activity of these neurons as recorded by extracellular electrophysiological techniques. This depressant effect was blocked by neuroleptic drugs and lithium, both of which also block the depressant effects of norepinephrine, but not those of GABA. PCP elicited depressions could not be obtained in rats in which the cerebellar noradrenergic terminals had been lesioned with 6-hydroxydopamine (6-OHDA). However, PCP was still an effective depressant in animals after destruction of nonnoradrenergic intrinsic excitatory and inhibitory interneurons which synapse on the Purkinje cell by neonatal X-irradiation. Further treatment of the X-irradiated animal with 6-OHDA resulted in Purkinje neurons which were not responsible to PCP. Administration of magnesium ions, which reduces the release of neurotransmitters from afferent terminals, also suggests that PCP acts in the cerebellum by a presynaptic mechanism involving release of norepinephrine from intact, functioning noradrenergic terminals. 30 references. (Author abstract modified)

003927 Marzullo, Giovanni; Friedhoff, Arnold J. Millhauser Laboratories, Psychiatry Dept., New York University School of Medicine, New York, NY 10016 **COMT-A and COMT-B: catalytic differences and role of disulfides bonds.** Research Report, NIMH Grant 5P01-MH-8618, 1980. 11 p.

Differences between the two principal forms of the enzyme catechol-0-methyltransferase (COMT-A and COMT-B) are described, and the mechanism which is involved in the production of different meta/para methylation ratios is examined. For analysis of meta/para methylation ratios, normal and isovanillic acids resulting from dihydroxybenzoate were separated by this layer chromatography. It appeared that the configuration of the catechol binding site of COMT-B differed from that of COMT-A in a way which resulted in a reduced probability of the catechol binding in a paramethylating orientation. The higher ability of COMT-B to methylate hydroxy groups adjacent to methoxy groups was also probably a reflection of the same configurational difference at the binding site. The SS bridge appeared to influence the configuration of the catechol binding site in a way that reduced the probability of the paramethylating binding mode. This same type of disulfide bridge appeared to form between enzyme nonomer and GSSG when homogenates were incubated with oxidized glutathione. 27 references.

003928 Masso, J. L.; Roberts, D. J. Roberts: Dept. of Pharmacology, Research Institute of Laboratorios Almirall, Cardoner 68-74, Barcelona, Spain **Comparison of the potencies of clebopride and other substituted benzamide drugs on isolated gastrointestinal tract of the guinea-pig and rat.** Journal of Pharmacy and Pharmacology. 32(10):727-728, 1980.

The effects of the substituted benzamides clebopride, metoclopramide, and sulpiride were studied in strips of rat gastric fundus and portions of guinea-pig ileum and colon. Clebopride induced dose-related contractions in all three preparations, as did 5-hydroxytryptamine (5-HT). Metoclopramide was weaker than clebopride in all three preparations, and sulpiride was active only in the ileum preparation. The ileum was the most sensitive and the colon the least sensitive to 5-HT and the substituted benzamides. Results indicate that clebopride is more potent than other substituted benzamide drugs in the gastrointestinal tract, which is consistent with previous findings in other models of CNS antidopaminergic activity. 18 references.

003929 Matthews, W. D.; McCafferty, G. P.; Setler, P. E. Dept. of Pharmacology, Smith Kline & French Laboratories, Philadelphia, PA 19101 **An electrophysiological model of GABA-mediated neurotransmission.** Neuropharmacology. 20(6):561-565, 1981.

Electrical stimulation of the perforant pathway in anesthetized male Sprague-Dawley rats resulted in excitation followed by inhibition of granule cells in the hippocampal dentate gyrus. Physiological, biochemical, and immunocytochemical evidence suggests that the inhibition of granule cell activity was mediated by recurrent collateral activation of an inhibitory GABA interneuron. The GABA antagonist bicuculline reduced recurrent inhibition in the dentate gyrus, whereas the GABA agonist, nipecotic acid, prolonged the inhibition. The GABA uptake inhibitors guvacine and L-2,4-diaminobutyric acid enhanced the duration of recurrent inhibition up to 75%. Strychnine had no effect on the duration of recurrent inhibition. Blockade of GABA synthesis with isoniazid markedly reduced or abolished the inhibition. Results indicate that recurrent inhibition in the dentate gyrus is mediated by synaptically released GABA and that uptake into neurons or glia limits its duration of action. 19 references. (Author abstract modified)

003930 Mautner, Henry G. Dept. of Biochemistry and Pharmacology, Tufts University School of Medicine, Boston, MA 02111 **Acetylcholine and choline acetyltransferase.** Neurochemistry International. 2(1/3):123-134, 1980.

The thermodynamics and kinetics of the alcoholysis of thiolesters are discussed in relation to choline acetyltransferase. The conformational and rotational barriers of acetylcholine are described, as is the specific inability of choline to induce depolarization. Evidence is presented for the involvement of imidazole and the lack of involvement of thiol groups in the active site of choline acetyltransferase. The interaction of coenzyme-A (CoA) and a series of CoA analogs and the interaction of dyes with the CoA binding site are discussed. The importance of the 3'-phospho group of CoA and an active site arginine for these interactions is emphasized. 75 references.

003931 Mayer, M. L.; Straughan, D. W. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **Effects of 5-hydroxytryptamine on central neurones antagonized by bicuculline and picrotoxin.** Neuropharmacology. 20(4):347-350, 1981.

In anesthetized Wistar rats, ionotophoretic application of bicuculline methochloride blocked the inhibitory effects of GABA and 5-hydroxytryptamine (5-HT) on 8 of 11 medial preoptic neurons. The inhibitory action of glycine was affected only slightly by bicuculline. The inhibitory effect of 5-HT on visual cortex neurons was blocked by applications of 5-HT or picrotoxin. Results suggest that 5-HT and GABA may act on the same receptor/effector complex in some neurons. 20 references. (Author abstract modified)

003932 Mazurkiewicz-Kwilecki, I. M. Dept. of Pharmacology, Faculty of Health Sciences, School of Medicine, University of Ottawa, 275 Nicholas St., Ottawa, Canada K1N 9A9 **Effect of diazepam on stress induced changes in brain histamine.** Pharmacology Biochemistry and Behavior. 14(3):333-338, 1981.

Acute treatment with diazepam (2.5, 5, and 10mg/kg orally) did not affect the basal concentration of histamine in the hypothalamus of male Sprague-Dawley rats. The increase in hypothalamic histamine induced by 15 minutes of platform stress was significantly attenuated by 5 or 10mg/kg diazepam, but the elevation induced by 15 minutes of air blasts was not altered. Diazepam significantly reduced the rise in plasma corticosterone concentration in response to air blast stress, but did not affect the increase caused by platform stress. 70 references. (Author abstract modified)

003933 McLennan, Peter L. Dept. of Pharmacology, Monash University, Clayton, Victoria, Australia, 3168 **The hypothermic effect of clonidine and other imidazolidines in relation to their ability to enter the central nervous system in mice.** European Journal of Pharmacology. 69(4):477-482, 1981.

The ability of clonidine and structurally related imidazolidines to enter the CNS was studied in female Swiss mice. All the imidazolidines tested caused dose dependent reductions in body temperature. The drug-induced hypothermia was inhibited by intracisternal (but not intraperitoneal) injections of piperoxan, an alpha-adrenoceptor antagonist. It is concluded that the test compounds all crossed the blood-brain barrier to interact with alpha-adrenoceptors and cause hypothermia. These findings suggest that the failure of some imidazolidines to cause sedation and hypotension is not due to an inability to penetrate the blood-brain barrier. 20 references. (Author abstract modified)

003934 Medvedev, B. A.; Mashkovskiy, M. D. Lab. farmakologii, Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonikidze, Moskva, USSR **/The effect of antidepressants on the hypotensive effect of clofelin in rats./** Vliyaniye antidepressantov na gipotenzivnyy effekt klofelina y krys. Farmakologiya i Toksikologiya. 43(4):374-376, 1980.

The effect of the antidepressants azaphen, pyrazidol, inkasan, imipramine, and amitriptyline on the hypotensive effect of clofelin was studied in unanesthetized rats with normal arterial blood pressure. Results show that the antidepressants reduced the hypotensive effect of clofelin. As the dosage was increased, the antidepressants themselves started to exert a hypotensive effect; but the antagonism to clofelin in relation to the arterial blood pressure was maintained. These results suggest that such an effect is due to the impairment of neuronal noradrenaline uptake, induced by the antidepressants. 12 references. (Journal abstract modified)

003935 Mefford, Ivan N.; Roth, Kevin A.; Gilberg, Mark; Barchas, Jack D. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **In vivo intraneuronal MAO inhibition in rat brain SKF 64139, comparison to other potent PNMT inhibitors.** European Journal of Pharmacology. 70(3):345-353, 1981.

Acute administration of the phenylethanolamine-N-methyltransferase inhibitor 7,8,dichloro-1,2,3,4-tetrahydroisoquinoline (SKF-64139) to male Sprague-Dawley rats increased brain serotonin levels and depleted brain levels of 5-hydroxyindolacetic acid, homovanillic acid, and 3,4-dihydroxyphenylacetic acid. Pretreatment with SKF-64139 antagonized the increase in acid metabolites and depletion of amines induced by reserpine. Results suggest that SKF-64139 may be a potent intraneuronal monoamine oxidase inhibitor. 14 references. (Author abstract modified)

003936 Messing, Rita B.; Vasquez, Beatriz J.; Samaniego, Bernardo; Jensen, Robert A.; Martinez, Joe L., Jr.; McGaugh, James L. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Alterations in dihydromorphine binding in cerebral hemispheres of aged male rats.** Journal of Neurochemistry. 36(2):784-787, 1981.

Equilibrium binding of 3H-dihydromorphine was assayed in brain regions of young and aged male F344 rats. Young rats had significantly higher receptor densities than old rats in the frontal poles, anterior cortex, and striatum. In the frontal poles, the aged related decline in receptor concentration was accompanied by a significant increase in the apparent affinity of dihydromorphine for receptors. This pattern of receptor alterations differs from that previously observed in aged female rats, suggesting possible sex differences in mechanisms underlying age related synaptic alterations. 18 references. (Author abstract modified)

003937 Meyer, E. M.; Cooper, J. R. Cooper: Dept. of Pharmacology, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **Correlations between Na-K ATPase activity and acetylcholine release in rat cortical synaptosomes.** Journal of Neurochemistry. 36(2):467-475, 1981.

The efflux of tritiated acetylcholine (3H-ACh) and the activity of the sodium/potassium (Na/K) stimulated ATPase ion pump were studied concomitantly in male Sprague-Dawley rat cortical synaptosomes. Ouabain, strophanthidin, and parachloromercuribenzene sulfonate inhibited ouabain sensitive rubidium (86Rb) uptake and elevated 3H-ACh release independently of the external calcium concentration. Veratridine, electrical field stimulation, and the calcium ionophore A23187 also inhibited ouabain sensitive 86Rb uptake and released 3H-ACh, but by a calcium dependent process. Veratridine-induced 3H-ACH release and ion pump inhibition were blocked by pretreatment with tetrodotoxin. Results suggest that 3H-ACh release is due at least in part to inhibition of Na/K stimulated ATPase. 33 references. (Author abstract modified)

003938 Mikuni, Masahiko; Saito, Yoshiro; Koyama, Tsukasa; Yamashita, Itaru. Dept. of Psychiatry and Neurology, Hokkaido University School of Medicine, North 15 West 7, Kita-ku, Sapporo, Hokkaido, Japan **Circadian variation of cyclic AMP in the rat pineal gland.** Journal of Neurochemistry. 36(3):1295-1297, 1981.

Cyclic AMP concentrations in the male Wistar-King pineal gland showed a distinct circadian variation, with the maximum level at 0200 at the lowest at 1400. Propranolol completely blocked the dark-induced increase in pineal cyclic AMP at 0200. Isoproterenol induced a rapid, threefold increase in cyclic AMP level at 1400, but had no effect at 0200. 26 references. (Author abstract modified)

003939 Miller, Jeannette C.; Friedhoff, Arnold J. Millhauser Laboratories, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **The effect of prenatal exposure to ethanol or opiates on brain catecholamine activity.** In: Parvez, H., Biogenic amines in development. Elsevier/North Holland, 1980. (p. 709-724).

A review is presented of the effects of prenatal exposure to ethanol and opiates, two classes of drugs of abuse, on central cholaminergic activity and related behaviors. Adverse clinical effects of ethanol exposure prenatally in human infants have analogues in animals prenatally exposed. Animal offspring exhibit decreased bodyweight, and decreased brain weight, and show impairments in learning ability and increased motor activity. Limited data do not permit definitive conclusions about the permanence of change in catecholamine synthesis in ethanol exposed offspring. In utero exposure to morphine or other narcotics results in growth retardation and behavioral disturbances in human infants. Growth retardation, postnatal mortality rate increases, tolerance to analgesic effects, disturbed mother-infant interaction, and dependence have been reported in prenatal exposure studies in the rat. Further, it is not unlikely that biochemical effects of opiates observed in treated adults would have similar effects on brain development of catecholaminergic systems and opioid peptide and receptor systems of prenatally and/or postnatally exposed animals. 96 references.

003940 Misra, Chandra H.; Smith, Robert C. Section of Biological Psychiatry, Texas Research Institute of Mental Science, 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Effects of age on dopaminergic supersensitivity induced by chronic fluphenazine.** Communications in Psychopharmacology. 4(5):411-415, 1980.

The influence of age on dopaminergic supersensitivity induced by chronic fluphenazine was investigated. Twenty-five-month-old Fisher 344 rats terminated from chronic administration of fluphenazine developed a 24% increase in specific binding of spiperone in the striatum (compared to age matched saline controls), similar to the increase observed in 7-month-old fluphenazine treated rats. The older fluphenazine treated rats had a slightly lower increase in the Bmax of spiperone binding than did the younger rats. The aging rat brain retains the capacity to develop a supersensitive response to chronic neuroleptic administration. 13 references. (Author abstract modified)

003941 Miyakoshi, Nobuhiro; Tanaka, Minoru; Shindo, Hideyo. Central Research Laboratories, Sankyo Co., Ltd., Hiromachi 1-2-58, Shinagawa-ku, Tokyo 140, Japan **Autoradiographic studies on distribution of L-3,4-dihydroxyphenylalanine (L-DOPA)-14C and L-5-hydroxytryptophan (L-5-HTP)-14C in the cat brain.** Japanese Journal of Pharmacology. 30(6):795-805, 1980.

Autoradiography and chromatography were used to study the distribution and metabolism of 14C-labeled L-DOPA and 5-hydroxytryptophan (5-HTP). An appreciable amount of radioactivity in the gray matter was found, but not in the white matter. After oral administration of L-DOPA-14C, radioactivity levels were high in the caudate nucleus, putamen, and pallidum. After i.v. administration of L-5-HTP-14C, radioactivity was high in the hypothalamus, raphe nucleus, substantia nigra, inferior olivalis, and caudate nucleus. After L-DOPA administration, high concentrations of dopamine were detected in the caudate nucleus and hypothalamus. After L-5-HTP administration, high concentrations of serotonin were detected in the hypothalamus and medulla oblongata. 18 references. (Author abstract modified)

003942 Morley, John E.; Brammer, Gary L.; Sharp, Burt; Yamada, Tadataka; Yuwiler, Arthur; Hershman, Jerome M. Brammer: Neurobiochemistry Research Laboratory T-85, VA Brentwood Medical Center, 11301 Wilshire Blvd., Los Angeles, CA 90073 **Neurotransmitter control of hypothalamic-pituitary-thyroid function in rats.** European Journal of Pharmacology. 70(3):263-271, 1981.

In a study of the role of monoamine neurotransmitters in the regulation of the hypothalamic/pituitary/thyroid axis, male Sprague-Dawley rats were treated acutely or chronically with neurotransmitter precursors (tryptophan and L-DOPA), synthesis inhibitors (p-chlorophenylalanine and alpha-methyltyrosine), uptake inhibitors (desipramine and zimelidine), or lithium carbonate. Hypothalamic levels of thyrotropin releasing hormone (TRH) and somatostatin-like immunoreactivity and serum levels of thyrotropin, thyroxine, and triiodothyronine were determined. Results suggested that TRH release is regulated by an excitatory noradrenergic system and by serotonergic and dopaminergic inhibitory systems. The serotonergic influence appeared to be a factor only after activation of the central serotonergic system. Lithium increased the level of TRH in the hypothalamus. 43 references. (Author abstract modified)

003943 Morley, John E.; Levine, Allen S. Neuroendocrine Research Laboratory, Minneapolis V.A. Medical Center, Minneapolis, MN 55417 **Intraventricular cholecystokinin-octapeptide**

produces hyperglycemia in rats. Life Sciences. 28(19):2187-2190, 1981.

Intraventricular administration of cholecystokinin-octapeptide (CCK-8) produced hyperglycemia in rats. A 250ng dose of CCK-8 increased plasma glycagon levels, but 2.5 and 25ng doses increased glucose without altering glucagon levels. Insulin levels were not altered by any dose of CCK-8 tested. A 14C-glucose tracer study showed that the hyperglycemia induced by CCK-8 was not due to alterations in glucose clearance. 14 references. (Author abstract modified)

003944 Morris, Margaret J.; Elghozi, Jean-Luc; Dausse, Jean-Pierre; Meyer, Philippe. Meyer: INSERM U7, Research Unit, Dept.of Nephrology, Hopital Necker, 161 rue de Sevres, F-75015 Paris, France **Alpha1- and alpha2-adrenoceptors in rat cerebral cortex: effect of frontal lobotomy.** Naunyn-Schmiedeberg's Archives of Pharmacology. 316(1):42-44, 1981.

Frontal lobotomy caused a reduction in the noradrenaline content of male Wistar rat cerebral cortex, indicating effective noradrenergic denervation. Changes in 3H-clonidine and 3H-prazosin binding after surgery revealed a reduction in the number of alpha2-adrenoceptors and a smaller but significant increase in the number of alpha1-adrenoceptors in the lesioned cortex. Results indicate that alpha2-adrenoceptors located on presynaptic noradrenergic terminals represent only a small proportion of the total alpha2-adrenoceptor population in the cerebral cortex. 22 references. (Author abstract modified)

003945 Nagy, A. no address **On the kinetics of imipramine and related antidepressants.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):147-156, 1980.

The kinetics of imipramine and related antidepressants are discussed. Several observations indicate that excessive demethylation can antagonize the therapeutic effect of antidepressants of the imipramine type. To date, there is no possibility of reducing demethylation other than by switching from oral to parenteral administration. Data are presented which indicate that treatment with imipramine-N-oxide does not increase the ratio between imipramine and desipramine in the plasma, but imipramine-N-oxide administration does increase this ratio in the blood cells and in the brain. A panel discussion of these topics is appended. 16 references.

003946 Nakadate, Teruo; Muraki, Takamura; Kato, Ryuichi. Dept. of Pharmacology, School of Medicine, Keio University, Shinanomachi, Shinjuku-ku, Tokyo 160, Japan **Effects of alpha- and beta-adrenergic blockers on chlorpromazine-induced elevation of plasma glucose and cyclic AMP in fed mice.** Japanese Journal of Pharmacology. 30(2):199-206, 1980.

Subcutaneous injection of chlorpromazine (CPZ) in fed male ddY mice caused dose dependent increases in plasma glucose and cyclic AMP levels, which were blocked by hexamethonium. Propranolol inhibited the increase in plasma cyclic AMP, but not the increase in plasma glucose. Phentolamine and yohimbine suppressed the elevation of plasma glucose, but not the increase in plasma cyclic AMP. Results indicate that CPZ-induced hyperglycemia is mediated via stimulation of alpha-adrenoceptors, whereas the CPZ-induced increase in plasma cyclic AMP is mediated via stimulation of beta-adrenoceptors. 37 references. (Author abstract modified)

003947 Nakamura, Kazuo; Okada, Toshikazu; Ishii, Hisae; Nakamura, Keiji. Department of Pharmacology, Nippon Roche Research Center, Kamakura 247, Japan **Differential effects of alpha-methyldopamine, clonidine and hydralazine on norepinephrine and epinephrine synthesizing enzymes in the brainstem nuclei of spontaneously hypertensive rats.** Japanese Journal of Pharmacology. 30(1):1-10, 1980.

Repeated administration of clonidine to spontaneously hypertensive rats (SHR) markedly lowered dopamine-beta-hydroxylase (DBH) activity in the locus coeruleus and increased it in the spinal intermediolateral column. Alpha-methyldopa tended to lower DBH activity in the medullary nucleus tractus solitarii and A1 cell areas. Clonidine-induced inhibition of 3H-norepinephrine binding to crude synaptic membranes of SHR or Kyoto Wistar control rats was seven times greater than that of alpha-methyl-norepinephrine. Clonidine and hydralazine lowered phenylethanolamine N-methyltrasferase (PNMT) activity in the nucleus hypothalamicus posterior of SHR to control levels. Clonidine, hydralazine, and alpha-methyldopa increased PNMT in the nucleaus paraventricularis. Peripherally active hydralazine increased PNMT activity in the NTS and reduced activity in the A1 cell of SHR to control level. 39 references. (Author abstract modified)

003948 Near, Joseph A.; Mahler, Henry R. Mahler: Dept. of Chemistry, Indiana University, Bloomington, IN 47405 **Dopamine receptors in subcellular fractions from bovine caudate: enrichment of (3H)spiperone binding in a postsynaptic membrane fraction.** Journal of Neurochemistry. 36(3):1142-1151, 1981.

Specific binding of tritiated dopamine, spiperone, and N-propylnorapomorphine (NPA) in subcellular fractions from bovine caudate nucleus was examined. All fractions contained at least two sets of specific binding sites for 3H-spiperone and a single class of high affinity sites for 3H-dopamine. At least two classes of receptors were labeled by 3H-NPA. The binding of 3H-spiperone in a postsynaptic membrane fraction extracted and separated from synaptic plasma membranes (SPM) was enriched two to threefold over that in unfractionated SPM, with concomitant decrease in 3H-dopmaine binding. The enrichment in spiperone receptors was almost entirely due to an increase in the number of low affinity binding sites, suggesting these sites are associated with the postsynaptic membrane. 41 references. (Author abstract modified)

003949 Neff, N. H.; Parenti, M.; Gentleman, S.; Olianas, M. C. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Modulation of dopamine receptors by opiates. (Unpublished paper).** Bethesda, MD, NIMH, 1980. 9 p.

Evidence is presented in support of the view that opiate receptors are in communication with the dopamine receptor complex and act as modulators of the responsiveness of the dopamine adenylate-cyclase system. Research using rat striatal membranes is cited to demonstrate that morphine inhibits dopamine activated adenylate-cyclase; and that opioid peptides, but not other neuropeptides, inhibit dopamine stimulated adenylate-cyclase. A simple model is proposed to explain similarities in pharmacology between neuroleptic drugs and narcotics. Both classes of compounds prevent dopamine stimulating its receptor. Neuroleptics displace dopamine from its receptor site, while opiates do not displace, but prevent dopamine from activating adenylate-cyclase, perhaps by interacting with the GTP binding site. Such a mechanism implies that endogenous opiate peptides play a physiological role in dampening dopamine receptor responsiveness. The model would also predict that chronic treatment with morphine produces supersensitivity of the dopamine adenylate-cyclase system. 16 references.

003950 Nimit, Y.; Skolnick, P.; Daly, J. W. Daly: Bldg. 4, Room 212, NIH, Bethesda, MD 20205 **Adenosine and cyclic AMP in rat cerebral cortical slices: effects of adenosine uptake**

inhibitors and adenosine deaminase inhibitors. Journal of Neurochemistry. 36(3):908-912, 1981.

The adenosine deaminase inhibitor 2'-deoxycoformycin (2'-DCF) slightly increased the basal, adenosine elicited, and norepinephrine elicited accumulations of cyclic AMP in male Sprague-Dawley rat cortical slices. Dipyridamole, an adenosine uptake inhibitor, had an even greater effect on cyclic AMP accumulations, and the effects of combinations of 2'-DFC and dipyridamole were greater than those of either compound alone. Neither agent signficantly augmented accumulations of cyclic AMP elicited by veratridine, a depolarizing agent. 20 references. (Author abstract modified)

003951 Nishi, Hiroyoshi; Watanabe, Shigenori; Ueki, Showa. Pharmacology Group, Research Laboratory, Mitsubishi Yuka Pharmaceutical Co. Ltd., Ami-cho, Ibaraki 300-03, Japan **Effect of median raphe stimulation on hippocampal seizure discharge induced by carbachol in the rabbit.** Japanese Journal of Pharmacology. 30(5):759-762, 1980.

Carbachol (5mcg) administered into the rabbit dorsal hippocampus elicited a seizure discharge, but this effect was not seen when carbachol was given after electrical stimulation of the median raphe nucleus. The inhibitory effect of raphe stimulation on carbachol discharge was completely blocked by pretreatment with p-chlorophenylalanine. Results suggest that serotonin released by raphe stimulation plays an inhibitory role in the manifestation of carbachol-induced hippocampal seizure discharge. 9 references.

003952 Nistico, G.; Ientile, R.; Rotiroti, D.; Lanotte, M.; Di Giorgio, R. M. Institute of Pharmacology, University of Messina, Messina, Italy **Evidence to suggest that dopamine-induced increase in GABA concentrations in chick brain is mediated through cyclic AMP.** Journal of Pharmacy and Pharmacology. 32(9):663-664, 1980.

Administration of (-)-dopa or apomorphine into the third cerebral ventricle of Rhode Island Red chicks significantly stimulated GABA synthesis in the diencephalon. Intracerebroventricular injection of dibutyryl cyclic AMP or adenosine in chicks pretreated with aminophylline also increased GABA content and glutamic acid decarboxylase (GAD) activity. Results indicate that GABA synthesis is increased in conditions of increased dopaminergic activity and suggest that dopamine receptors coupled to adenylate cyclase may regulate GAD activity. 21 references.

003953 O'Fallon, James V.; Brosemer, Ronald W.; Harding, Joseph W. Harding: Dept. of Veterinary and Comparative Anatomy, Washington State University, Pullman, WA 99164 **The Na,K-ATPase: a plausible trigger for voltage-independent release of cytoplasmic neurotransmitters.** Journal of Neurochemistry. 36(2):369-378, 1981.

The release of neurotransmitters from eight regions of male Swiss-Webster mouse brain in response to 60mM potassium or 20mcM ouabain, a specific inhibitor of sodium/potassium stimulated adenosine triphophatase, was studied. Potassium was superior to ouabain in releasing biogenic amines. Putative amino acid transmitters generally were released by both agents. The pattern of release suggested that potassium initiated the release of transmitter from both vesicular and cytoplasmic pools, while ouabain stimulated stimulated release only from the cytoplasm in a voltage independent manner. 69 references. (Author abstract modified)

003954 Osborne, Neville N. Nuffield Laboratory of Ophthalmology, University of Oxford, Walton St., Oxford OX2 6AW, England **Binding of (3H)-muscimol, a potent gamma-aminobutyric acid receptor agonist, to membranes of the bovine retina.** British Journal of Pharmacology. 71(1):259-264, 1980.

The binding of 3H-muscimol to crude membrane preparations of bovine retina was studied, using a filtration method to isolate membrane bound ligand. Specific binding was saturable and occurred at two binding sites with affinity constants of 4.3nM and 38.2nM. Binding was sodium independent, enhanced by freezing or Triton-X-100 treatment, and abolished by sodium laurylsulphate. The binding sites showed a high degree of pharmacological specificity; GABA was a potent displacer of 3H-muscimol. Specific 3H-muscimol binding was greater in subcellular fractions enriched with photoreceptor synaptosomes than in fractions enriched with conventional synaptosomes. 20 references. (Author abstract modified)

003955 Palkovits, Miklos; Raisman, Rita; Briley, Michael; Langer, Salomon Z. Langer: LERS, Synthelabo, Dept. of Biology, 58 Rue de la Glaciere, F-75013 Paris, France **Regional distribution of (3H)imipramine binding in rat brain.** Brain Research. 210(1-2):493-498, 1981.

The binding of 3H-imipramine in 23 microdissected areas of male Sprague-Dawley rat brain was compared with published values for endogenous levels of serotonin, noradrenaline, and dopamine in these areas. The density of 3H-imipramine binding sites was highly correlated with the distribution of endogenous serotonin, especially serotonin localized in nerve terminals. The distribution of 3H-imipramine binding was weakly correlated with the distribution of endogenous noradrenaline, but showed no correlation with the distribution of endogenous dopamine. 22 references. (Author abstract modified)

003956 Palmer, Gene C.; Palmer, S. Jo; Legendre, Janet L. Dept. of Pharmacology, University of South Alabama College of Medicine, Mobile, AL 36688 **Guanylate cyclase--cyclic GMP in mouse cerebral cortex and cerebellum: modification by anticonvulsants.** Experimental Neurology. 71(3):601-614, 1981.

The modification by anticonvulsants of guanylate cyclase and cyclic GMP was studied in mouse cerebral cortex and cerebellum preparations. Incubated tissue slices readily accumulated cyclic GMP in response to challenge by ouabain, NaN3, NH2OH, or KCl, but not l-glutamate, l-aspartate, glycine, GABA, kainic acid, and the calcium ionophore, A-23187. Inhibition of the ouabain-induced accumulation of cyclic GMP was evident with valproate, carbamazepine, clonazepam, phenytoin, and phenobarbital. Only phenytoin blocked the action of KCl, and cyclic GMP responses to NaN3 were inhibited by high concentrations of valproate, carbamazepine, phenytoin, or phenobarbital. Results suggest that anticonvulsant drug actions with regard to central cyclic GMP systems are related to the Na-induced depolarization of nerve tissue and not to any direct action on the guanylate cyclase enzyme. 33 references. (Author abstract modified)

003957 Palmer, Michael R.; Hoffer, Barry J. Dept. of Pharmacology, C236, University of Colorado Health Sciences Center, 4200 E. Ninth Avenue, Denver, CO 80262 **Catecholamine modulation of enkephalin-induced electrophysiological responses in cerebral cortex.** Journal of Pharmacology and Experimental Therapeutics. 213(2):205-215, 1980.

The interaction between locally applied D-Ala2-methionine enkephalinamide (2dA) and catecholamine inputs to frontal cortex was investigated in rats. Parenteral administration of antipsychotic agents known to block catecholamine receptors, such as spiroperidol, alpha-flupenthixol, and ()-butaclamol, reversibly antagonized enkephalin-induced depressions. The biochemically inactive isomers of these antipsychotics, beta-flupenthixol, and (-)-butaclamol, manifested no such activity. Unilateral lesions of the catecholaminergic projections to frontal cortex, produced by interstitial injection of 6-hydroxydopamine, resulted in an ipsilateral decrease in 2dA efficacy and in an elimination of the antogonisms of 2dA depressions by antipsychotic agents. The depressions caused by 2dA were not antagonized by iontophoretically applied Mg. It is concluded that intact catecholaminergic transmissions are required for the full expression of enkephalin-induced depressions in frontal cortex and that this mechanism probably does not involve presynaptic release. These results suggest that catecholamines may act as postsynaptic modulators to augment responsiveness to enkephalins. 66 references. (Author abstract modified)

003958 Parenti, M.; Gentleman, S.; Olianas, M. C.; Neff, N. H. Laboratory of Preclinical Pharmacology, WAW 134, St. Elizabeths Hospital, Washington, DC 20032 **The dopamine receptor complex: biochemical consequences of supersensitivity induced by treatment with 6-hydroxydopamine or morphine.** Washington, DC, NIMH, 1980. 7 p.

The biochemical consequences which occur when dopamine receptors become supersensitive by treatment with 6-hydroxydopamine (6-OHDA) or morphine were investigated to further investigate CNS adaptive mechanisms for maintaining neurochemical homeostasis in the rat. Evidence is presented to support the hypothesis that common biochemical mechanisms are responsible for the dopamine activated adenylate-cyclase supersensitivity induced by denervation with 6-OHDA and morphine dependence. The changes are apparently the result of a decreased ability of dopamine to interact favorably with its receptor complex in vivo. Denervation decreases the quantity of dopamine released by nerve impulses, while morphine prevents dopamine from activating adenylate-cyclase. The mechanisms for development of supersensitivity are unclear, but the findings indicate that supersensitivity is clearly the consequence of integrated changes of the receptor complex. 9 references. (Author abstract modified)

003959 Patrick, Robert L. Box G, Division of Biology and Medicine, Brown University, Providence, RI 02912 **Phenylethylamine effects on dopamine synthesis: structure-activity relationships. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-31706, 1980. 21 p.

The effects of substituents on phenylethylamine and amphetamine-induced alterations in dopamine synthesis were studied in rat brain synaptosomal preparations isolated from the corpus striatum. The synthesis stimulation normally observed with phenylethylamine and amphetamine was converted into an inhibition by the addition of a p-hydroxy substituent on the ring. B-hydroxy substitution on the side chain somewhat lowered, but did not prevent, synthesis stimulation; the presence of both a B-hydroxy and p-hydroxy substituent increased the inhibitory effects, with 45% inhibition produced by 20 mcM dl-octopamine and 50% inhibition produced by 20 mcM dl-p-hydroxynorephedrine. The addition of an N-methyl substituent on d-amphetamine to form d-methamphetamine did not alter significantly the stimulatory potency of amphetamine. Tyramine-induced synthesis inhibition was prevented by preincubation with cocaine. Amphetamine antagonized the synthesis stimulation produced by the depolarizing agent veratridine, but tyramine did not have this effect. These findings suggest that the parent phenylethylamine compounds interact with an intracellular regulatory site, possibly related to calcium flux and/or dopamine release, that is not affected by the p-hyroxy derivatives. 28 references. (Author abstract modified)

003960 Patrick, Robert L.; Berkowitz, Alan L.; Regenstein, Anne C. Neuroscience Section, Division of Biology and Medicine, Brown University, Providence, RI 02912 **Effects of in vivo amphetamine administration on dopamine synthesis regulation in rat brain striatal synaptosomes. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-31706, 1980. 26 p.

The stimulation of dopamine synthesis in rat brain striatal synaptosomes produced by the depolarizing agent veratridine is reduced markedly by prior in vivo amphetamine administration. The effect apparently was not due to an interference with the depolarization process per se, since veratridine-induced inhibition of tyrosine uptake, a biochemical correlate of depolarization, was unaffected by amphetamine. Antagonism of veratridine-induced synthesis stimulation was not duplicated by an in vivo treatment with pargyline, apomorphine, gamma-butyrolactone, or haloperidol, suggesting that this effect may be due to a direct cellular action of amphetamine. In vitro amphetamine-induced synthesis stimulation was not reduced, but this stimulation was altered in character and was no longer calcium dependent. A similar loss of calcium dependency was observed following in vivo reserpine treatment. These results suggest in vivo amphetamine treatment can markedly alter the interactions between tyrosine hydroxylase and synaptosomal dopamine pools that may be involved in regulation of catecholamine formation. 44 references. (Author abstract modified)

003961 Patsalos, P. N.; Lascelles, P. T. Dept. of Neurobiology and Anatomy, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **Changes in regional brain levels of amino acid putative neurotransmitters after prolonged treatment with the anticonvulsant drugs diphenylhydantoin, phenobarbitone, sodium valproate, ethosuximide, and sulthiame in the rat.** Journal of Neurochemistry. 36(2):688-695, 1981.

The effects of 10 day treatment with anticonvulsant drugs on regional brain concentrations of amino acid neurotransmitters were studied in male Wistar rats. Diphenylhydantoin significantly reduced cerebellar GABA, taurine, and aspartate and hypothalamic GABA and aspartate. Sodium valproate significantly elevated GABA and taurine in most regions. Phenobarbitone significantly elevated GABA in all brain regions and increased taurine in the cerebral cortex. Ethosuximide induced relatively small changes. Complex changes were seen after sulthiame or combinations of anticonvulsants. 48 references. (Author abstract modified)

003962 Paul, Steven M.; Rehavi, Moshe; Rice, Kenner C.; Ittah, Yitzhak; Skolnick, Phil. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Does high affinity (3H) imipramine binding label serotonin reuptake sites in brain and platelet?** Life Sciences. 28(24):2753-2760, 1981.

To establish whether high affinity (3H)imipramine binding sites (recently demonstrated in membrane preparations from rat brain, human platelet, and human brain) are associated with either platelet or neuronal uptake of serotonin, the relative potencies of a series of tricyclic antidepressants in inhibiting (3H)imipramine binding and serotonin uptake were determined under identical assay conditions. A close correlation between inhibition of serotonin uptake and (3H)imipramine binding was observed. In addition, electrolytic lesions of the midbrain raphe produced a decrease in (3H)imipramine binding in hypothalamic synaptosomes that paralleled the decrease in (3H)serotonin uptake. Finally, incubation of synaptosomal membranes with 2,8-dinitroimipramine, an irreversible inhibitor of (3H) imipramine binding, produced a dose dependent decrease in serotonin uptake, without altering the uptake of norepinephrine or dopamine. Results strongly suggest that high affinity binding of (3H)imipramine selectively labels serotonin uptake sites in brain and platelet. 19 references. (Author abstract modified)

003963 Perkins, M. N.; Stone, T. W. Dept. of Physiology, St. George's Hospital Medical School, University of London, London SW17 ORE, England **4-Aminopyridine blockade of neuronal depressant responses to adenosine triphosphate.** British Journal of Pharmacology. 70(3):425-428, 1980.

Microiontophoretic application of adenosine, adenosine monophosphate, and adenosine triphosphate depressed the firing rate of neurons in the male Porton Wistar rat cerebral cortex. Similar application of 4-aminopyridine blocked the depressant effects of the purines without affecting responses to GABA. This blockade was effected against purine depressions of spontaneous as well as glutamate evoked activity, which suggests the interaction occurred postsynaptically. 31 references. (Author abstract modified)

003964 Peroutka, Stephen J.; Snyder, Solomon H. Snyder: Dept. of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Regulation of serotonin2 (5-HT2) receptors labeled with (3H)spiroperidol by chronic treatment with the antidepressant amitriptyline.** Journal of Pharmacology and Experimental Therapeutics. 215(3):582-587, 1980.

Regulation of serotonin2 (5-HT2) receptors labeled with (3H)spiroperidol by chronic amitriptyline treatment was investigated. Chronic but not acute treatment with the tricyclic antidepressant amitriptyline reduced binding to 5-HT2 receptors by (3H)spiroperidol and beta-adrenergic receptor binding of (3H)dihydroalprenolol in brain membranes. The decrease is time dependent, gradually reversible, and represents a change in the number of binding sites with no alteration in drug affinities for 5-HT2 receptors. The effect can be observed at daily doses of 2.5mg/kg, similar to clinically effective doses in humans. At all doses and time intervals, the decrease in 5-HT2 receptors is more marked than the concurrent change in total beta-adrenergic receptor binding. The properties of 5-HT2 receptor reduction after chronic antidepressant treatment indicate that this alteration could be associated with therapeutic response. 29 references. (Author abstract modified)

003965 Persson, Bengt; Henning, Matts. Dept. of Pharmacology, Fack, S-400 33 Goteborg, Sweden **Central cardiovascular and biochemical effects of baclofen in the conscious rat.** Journal of Pharmacy and Pharmacology. 32(6):417-422, 1980.

Baclofen (1.25 to 10mg/kg i.p.) elicited dose dependent increases in blood pressure and heartrate in conscious male Sprague-Dawley rats. Similar responses were observed after intracisternal or intracerebroventricular administration of 0.125 to 1mcg/kg baclofen. The cardiovascular effects of i.p. baclofen were antagonized by pretreatment with phenoxybenzamine, bethanidine, or hexamethonium and were significantly attenuated by combined pretreatment with alpha-methyl-m-tyrosine and alpha-methyl-p-tyrosine. Responses to baclofen were not affected by bilateral adrenal demedullation but were abolished by pentobarbitone anesthesia. At i.p., doses used in the circulatory studies, baclofen increased endogenous concentrations of brain dopamine and decreased dopamine utilization, but only slightly affected brain norepinephrine concentration and utilization. 34 references. (Author abstract modified)

003966 Petersen, Erling N. Dept. of Pharmacology, A/S Ferrosan, Sydmarken 5, DK-2860 Soeborg, Denmark **Pre- and postsynaptic alpha-adrenoceptor antagonism by neuroleptics in vivo.** European Journal of Pharmacology. 69(4):399-405, 1981.

The antagonistic actions of neuroleptics at presynaptic alpha-adrenoceptors of the sympathetic nerves to rat heart and at postsynaptic alpha-adrenoceptors in the systemic vascular circulation of rats were studied. Yohimbine (0.1mg/kg) was more active at presynaptic receptors than at postsynaptic receptors, whereas the reverse was true for prazosin (0.02 to 5mg/kg). Phentolamine (1 to 5mg/kg) was very active at both receptors. Melperone, haloperidol, thioridazine, and flupenthixol (0.1 to 5mg/kg) were more selective antagonists at postsynaptic alpha-adrenoceptors than prazosin. Clozapine, chlorpromazine, and chlorprothixene (0.1 to 5mg/kg) were antagonists at both types of receptors. It is suggested that neuroleptics with presynaptic alpha-adrenoceptor antagonism may enhance the activity of beta-adrenergic systems indirectly in peripheral organs and in the CNS. 15 references. (Author abstract modified)

003967 Peyer, Mark; Pletscher, Alfred. Pletscher: Dept. of Research, University Clinics, Kantonsspital Basel, CH-4031 Basel, Switzerland **Liberation of catecholamines and 5-hydroxytryptamine from human blood-platelets.** Naunyn-Schmiedeberg's Archives of Pharmacology. 316(1):81-86, 1981.

The release of 3H-dopamine, 3H-noradrenaline, and 14C-5-hydroxytryptamine from normal and reserpinized human blood platelets was examined. The effects of thrombin and various amine releasing drugs on platelets were compared with reported drug effects on monoaminergic neurons. Results indicate that platelets are not a completely satisfactory model for monoaminergic neurons, particularly catecholaminergic neurons. 21 references. (Author abstract modified)

003968 Philippu, Athineos; Dietl, Hans; Eisert, Albert. Institut fur Pharmakologie und Toxikologie der Universitat Wurzburg, Versbacher Strasse 9, D-8700 Wurzburg, West Germany **Hypotension alters the release of catecholamines in the hypothalamus of the conscious rabbit.** European Journal of Pharmacology. 69(4):519-523, 1981.

The effects of changes in blood pressure on the release of catecholamines in the hypothalamus of conscious, freely moving rabbits were examined. After the posterior hypothalamic nucleus was superfused with cerebrospinal fluid, an i.v. injection of nitropurisside elicited a fall of arterial blood pressure and an increase in the rates of release of endogenous catecholamines in the posterior hypothalamic nucleus. Noradrenaline increased blood pressure but did not alter the release of catecholamines. Results suggest that hypotension leads to a counteracting increase in the release of catecholamines in the posterior hypothalamus. 4 references. (Author abstract modified)

003969 Phillis, J. W.; Jiang, Z. G.; Chelack, B. J. Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatechwan S7N OWO, Canada **Effects of ethanol on acetylcholine and adenosine efflux from the in vivo rat cerebral cortex.** Journal of Pharmacy and Pharmacology. 32(12):871-872, 1980.

Ethanol significantly depressed the efflux of acetylcholine from male Sprague-Dawley and Wistar rat cortex, but did not significantly alter the efflux of adenosine and its metabolites. Results suggest that the central actions of ethanol may be mediated by cholinergic rather than purinergic mechanisms. 19 references.

003970 Poddar, Mrinal K.; Dewey, William L. Dewey: Dept. of Pharm., Medical College of Virginia, Virginia Commonwealth University, Box 613, MCV Station, Richmond, VA 23298 **Effects of cannabinoids on catecholamine uptake and release in hypothalamic and striatal synaptosomes.** Journal of Pharmacology and Experimental Therapeutics. 214(1):63-67, 1980.

The effects of delta9-tetrahydrocannabinol (delta9-THC), delta8-tetrahydrocannabinol (delta8-THC), cannabinol (CBN), and cannabidiol (CBD) on the uptake and release of tritiated dopamine (DA) and norepinephrine (NE) from synaptosomes from male Sprague-Dawley rat corpus striatum and hypothalamus were examined. Delta9-THC and delta8-THC had biphasic effects on uptake and release of DA and NE in both tissues. Low concentrations of delta9-THC and delta8-THC stimulated uptake of DA and NE and inhibited their release; high concentrations inhibited uptake and stimulated release. High concentrations of CBN and CBD inhibited uptake and stimulated release of DA and NE in both brain regions; no significant effects were observed with low concentrations of CBN or CBD. 27 references. (Author abstract modified)

003971 Pokorski, M.; Grieb, P.; Wideman, J. Institute for Environmental Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Opiate system influences central respiratory chemosensors.** Brain Research. 211(1):221-226, 1981.

When applied to the intermediate chemosensitive areas of the ventrolateral medulla of pentobarbitone anesthetized cats, fentanyl depressed ventilation and naloxone stimulated ventilation. These responses could not be evoked from neighboring areas. Results suggest that endogenous opiates are involved in the central regulaton of respiration. 19 references.

003972 Polesskaya, M. M.; Yumatov, Ye. A. Lab. emotsiy i emotsional'nykh stressov, NII normal'noy fiziologii imeni P. K. Anokhina, AMN SSSR, Moskva, USSR **/Convergent properties and chemical sensitivity of midbrain reticular formation neurons of unanesthetized rabbits./** Konvergentnyye svoystva i khimicheskaya chuvstvitel'nost' neyronov retikulyarnoy formatsii srednego mozga nenarkotizirovannykh krolikov. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova. 66(9):1319-1324, 1980.

Convergent properties and chemical sensitivity of midbrain reticular formation neurons were studied in 38 unanesthetized and nonimmobilized rabbits. A stimulating macroelectrode was implanted in the region of the ventromedial hypothalamus. Using a multichannel glass microelectrode the impulse activity of individual neurons of the midbrain reticular formation was recorded extracellularly, and biologically active substances were applied electrophoretically. Neuronal responses of the midbrain reticular formation to light and sound stimuli and to biologically negative stimuli (electrical skin stimulation and stimulation of the ventromedial hypothalamus) were compared to neuronal sensitivity to microiontophoretic administration of acetylcholine, noradrenaline, and serotonin. Results show that the reticular neurons have interrelated convergent and chemical properties, which suggest the neurochemical maintenance of the integrative activity of these neurons. However, results show no significant correlation between neuronal responses to particular types of stimulation and neuronal sensitivity to a particular transmitter. 13 references. (Journal abstract modified)

003973 Pong, Sheng-Shung; Wang, Ching C.; Fritz, Lawrence C. Merck Institute for Therapeutic Research, Rahway, NJ 07065 **Studies on the mechanism of action of avermectin B1a: stimulation of release of gamma-aminobutyric acid from brain synaptosomes.** Journal of Neurochemistry. 34(2):351-358, 1980.

Avermectin-B1a, a novel macrocyclic lactone antiparasitic agent, caused a marked and sustained increase of gamma-aminobutyric acid release from rat brain synaptosomes. A concentration of 8mcM to 10mcM of avermectin-B1a produced the maximal effect, while the half maximal level was achieved at 2mcM to 3mcM. The drug also stimulated gamma-aminobutyric acid release from synaptosomes in calcium free medium, which was 28% lower than that in the 1.8mM Ca2 medium. The compound did not, however, affect the synaptosomal release of glutamate. At the lobster neuromuscular junction, avermectin-B1a reduced the input resistance of muscle fibers in control Ringer's solution as well as in Ringer's solution in which Co2 was substituted for Ca2. This observation is in accordance with the Ca2 independent stimulation of gamma-aminobutyric acid release seen with synaptosomes. A good correlation between antiparasitic activity and gamma-aminobutyric acid releasing activity has been found among various derivatives of avermectin-B1a, which suggests that the ability of the drug to release its neurotransmitter may be the basis of its antiparasitic action. 29 references. (Author abstract modified)

003974 Preskorn, Sheldon H.; Hartman, Boyd K.; Raichle, Marcus E.; Clark, H. Brent. Dept. of Psychiatry, 4940 Audubon Avenue, Washington University School of Medicine, St. Louis, MO 63110 **The effect of dibenzazepines (tricyclic antidepressants) on cerebral capillary permeability in the rat in vivo.** Journal of Pharmacology and Experimental Therapeutics. 213(2):313-320, 1980.

The effects of dibenzazepines on cerebral capillary permeability were investigated in the rat in vivo. The degree of equilibration of (3H)water across the cerebral capillary was evaluated by measuring its cerebral extraction fraction (Ew) using a dual label radiactive tracer technique. All tricyclic antidepressants increased Ew as compared to base line. The rank order of the drugs in producing this response was doxepin greater than amitriptyline greater than imipramine greater than notriptyline greater than desmethylimipramine greater than protriptyline. The effect of amitriptyline, the prototype tricyclic for this study, was rapid in onset, reversible, dose dependent, and generalized throughout the brain. Amitriptyline also induced a marked increase in the cerebral extraction fraction of (3H)ethanol. A difference in the time course of the drug effect on these two tracers indicates that the elevation in Ew is due to the increase in cerebral capillary permeability to both polar and lipid soluble substances. Results demonstrate that tryicyclic antidepressants have important central effects on nonneuronal tissue. 28 references. (Author abstract modified)

003975 Propst, Friedrich; Hamprecht, Bernd. Hamprecht: Institut fur Physiologische Chemie der Universitat, Koellikerstr. 2, D-8700 Wurzburg, West Germany **Opioids, noradrenaline and GTP analogs inhibit cholera toxin activated adenylate cyclase in neuroblastoma x glioma hybrid cells.** Journal of Neurochemistry. 36(2):580-588, 1981.

Adenylate-cyclase in homogenates of neuroblastoma/glioma hybrid cells was inhibited by D-Ala2-Met5-enkephalin, morphine, and noradrenaline in a dose dependent manner, even after preactivation of the enzyme by cholera toxin. The effect of D-Ala2-Met5-enkephalin on cholera toxin activated enzyme was immediate in onset and rapidly reversed by naloxone. Guanyl-5'-yl-imidodiphosphate (GppNHp) stimulated basal enzyme activity, but inhibited enzyme activity activated by cholera toxin or prostaglandin-E1; stimulation occurred at concentrations of 100mcM or above, but inhibition occurred at concentrations as low as 0.1mcM. The inhibitory effect of GppNHp was antagonized by GTP. Results suggest that two separate guanyl nucleotide binding sites associated with adenylate-cyclase in the hybrid cells may mediate stimulation and inhibition of the enzyme by hormones. 42 references. (Author abstract modified)

003976 Pycock, C. J.; Horton, R. W. Dept. of Pharmacology, Medical School, University of Bristol, Bristol, England **Dopamine-dependent hyperactivity in the following manipulation of GABA mechanisms in the region of the nucleus accumbens.** Journal of Neural Transmission. 245:17-33, 1979.

The effect of manipulation of gamma-aminobutyric acid (GABA) mechanisms in the region of the nucleus accumbens on dopamine dependent locomotor hyperactivity in the rat was studied. Two models of hyperactivity were used: the injection of dopamine into the region of the nucleus accumbens in nialamide pretreated animals and the systemic administration of d-amphetamine. Both GABA and the GABA agonist 3-aminopropane sulphonic acid depressed hyperactivity in a dose related manner. GABA receptor antagonism with low doses of either picrotoxin or bicuculline enhanced the mild locomotor response induced by a low dose of dopamine injected into the nucleus accumbens; higher doses of the GABA antagonists resulted in varying degrees of generalized seizures. Blockade of GABA uptake systems with cis-1,3-aminocyclohexane carboxylic acid, nipecotic acid, or beta-alanine within the region of the nucleus accumbens produced dose related depression of dopamine dependent hyperactivity in both models. The results demonstrate an inhibitory action of GABA and drugs facilitating GABAergic transmission on dopamine dependent hyperactivity in the rat. (Journal abstract modified)

003977 Quirce, Carlos M.; Odio-Yglesias, Mauricio; Solano-N., Jose M.; Maickel, Roger P. Lab. de Investigacion en Neurociencias, Facultad de Farmacia, Universidad de Costa Rica, Ciudad Universitaria Rodrigo Facio, Costa Rica **/Nonuniform reactions in the general adaptation syndrome./** Reacciones no uniformes del sindrome general de adaptacion. Revista Latinoamericana de Psicologia. 13(1):37-50, 1981.

Adult male Swiss Webster mice were subjected to acute, repetitive, and repetitive acute sessions of cold exposure, immobilization, and i.p. administration of d-amphetamine sulfate. Blood plasma levels of corticosterone, glucose, and free fatty acids were assayed for all the conditions tested. The metabolic effects were found to be similar only as regarded the mobilization of corticosterone during acute applications of the three stressors. The differences observed contradict the traditional concepts of stressor nonspecificity and general adaptation syndrome uniformity. 12 references. (Author abstract)

003978 Quirce, Carlos M.; Odio, Mauricio; Maickel, Roger P. Laboratorio de Neurociencias, Facultad de Farmacia, Universidad de Costa Rica, San Jose, Costa Rica **Stress-modulated alteration of brain biogenic amines in the rat: effects of L-tryptophan.** Communications in Psychopharmacology. 4(5):371-377, 1980.

The effect of L-tryptophan on stress modulated alteration of brain biogenic amines in the rat was investigated. Subjecting adult male rats to periods of restraint stress according to an irregular/unpredictable schedule led to a significant decrease in whole brain levels of dopamine and significant increases in whole brain levels of norepinephrine and serotonin. Administration of L-tryptophan on a similar irregular schedule had no effect on brain dopamine, but it lowered brain norepinephrine and raised brain serotonin. Combined treatment with L-tryptophan and restraint stress resulted in brain levels of all three biogenic amines that were virtually identical to nonhandled control rats. 32 references. (Author abstract modified)

003979 Rabin, Richard A.; Wolfe, Barry B.; Dibner, Mark D.; Zahniser, Nancy R.; Melchior, Christine; Molinoff, Perry B. Molinoff: University of Colorado Health Science Center, Dept. of Pharmacology, 4200 E. Ninth Ave., Denver, CO 80262 **Effects of ethanol administration and withdrawal on neurotransmitter receptor systems in C57 mice.** Journal of Pharmacology and Experimental Therapeutics. 213(3):491-496, 1980.

Male C57BL/6 mice treated with ethanol for 7 days and withdrawn from ethanol for 24 hours showed a decreased hypothermic response to apomorphine, suggesting altered dopaminergic function. However, basal and dopamine stimulated adenylate cyclase activity in striatal homogenates from treated animals was not altered. No change in the affinity of apomorphine for the dopamine receptor or in the density or affinity of receptors for 3H-spiroperidol was found. Adrenergic receptor mediated accumulation of cyclic AMP in slices of cerebral cortex was not altered. However, the density of beta-2 adrenergic receptors decreased significantly in ethanol treated mice and in withdrawn mice. The density of muscarinic cholinergic receptors in the hippocampus and cerebral cortex was significantly increased after ethanol administration, but this effect was not observed after 24 hour withdrawal. 37 references. (Author abstract modified)

003980 Rando, Robert R.; Bangerter, Faan Wen; Farb, David H. Dept. of Pharmacology, Harvard Medical School, Boston, MA 02115 **The inactivation of gamma-aminobutyric acid transaminase in dissociated neuronal cultures from spinal cord.** Journal of Neurochemistry. 36(3):985-990, 1981.

Dissociated cell cultures from chick embryo spinal cord were able to synthesize GABA from added glutamate in a glutamate decarboxylase dependent reaction. A functional GABA transaminase in these cultures could be blocked by gabaculine, leading to an increase in GABA levels. Long-term (16 day) incubation with gabaculine in the medium did not appear to alter high affinity GABA transport in these cultures, which suggests the drug is not toxic to cells capable of accumulating GABA. 12 references. (Author abstract modified)

003981 Rebec, George V.; Alloway, Kevin D.; Curtis, Stephen D. Dept. of Psychology, Indiana University, Bloomington, IN 47405 **Apparent serotonergic modulation of the dose-dependent biphasic response of neostriatal neurons produced by d-amphetamine.** Brain Research. 210(1-2):277-289, 1981.

Amphetamine-induced changes in unit activity in the anterior neostriatum were studied in male Sprague-Dawley rats 48 hours after i.p. injection of 300mg/kg para-chlorophenylalanine (PCPA) or vehicle. An i.p. injection of 1.0mg/kg d-amphetamine inhibited neostriatal activity in vehicle controls, but produced prolonged excitation in rats treated with PCPA. A 7.5mg/kg dose of d-amphetamine produced a pronounced increase in firing rate in controls, which was significantly reduced by PCPA pretreatment. PCPA produced a significant reduction in serotonin, but not dopamine or norepinephrine, in the telencephalon. 55 references. (Author abstract modified)

003982 Redmond, D. Eugene, Jr. Clinical Research Unit, Connecticut Mental Health Center, New Haven, CT 06510 **Clonidine and the primate locus coeruleus: evidence suggesting anxiolytic and anti-withdrawal effects. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-31176, 1979. 38 p.

The effects of clonidine on locus coeruleus (LC) associated behaviors in the primate were investigated, and evidence is provided which suggests that both clonidine and opioids block LC stimulation effects. A brain alarm system is proposed which is activated by fear provoking stimuli and by opiate withdrawal. The anxiolytic effects of clonidine were demonstrated, and suggestions are made for other psychiatric and medical conditions (in addition to drug withdrawal syndromes and anxiety) in which anxiety may contribute to dysfunction and morbidity and in which clonidine may have ameliorative effects (Gilles de la Tourette syndrome, migrane headache, and arteriosclerotic cardiovascular disease). The research indicates that the norepinephrine system is involved in fear and anxiety, and in mediating the actions of opioids and endorphins. The use of clonidine pharmacotherapy involves utilization of anatomically and neurophysiologically characterized receptors to produce the desired specific effects on norepinephrine systems predicted to be effective in reducing anxiety. 110 references.

003983 Reimann, Wolfgang; Steinhauer, Hjalmar B.; Hedler, Liselotte; Starke, Klaus; Hertting, Georg. Pharmakologisches Institut, Universitat Freiburg, Hermann-Herder-Strasse 5, D-7800 Freiburg i. Br., West Germany **Effect of prostaglandins D2, E2 and F2alpha on catecholamine release from slices of rat and rabbit brain.** European Journal of Pharmacology. 69(4):421-427, 1981.

The effects of prostaglandins (PGs) on catecholamine release were studied in slices of rabbit or male Wistar rat brain cortex preincubated with (3H)noradrenaline and slices of rabbit caudate nucleus or rat striatum preincubated with (3H)dopamine. PGE2 (0.01 to 1mcmol/l) markedly reduced the overflow of tritium evoked by electrical stimulation of rat cortex slices. PGF2alpha (1mcmol/l) caused slight decrease, but only after the formation of endogenous prostaglandins was blocked by indomethacin. PGD2 (1mcmol/l) had no effect. None of the PGs caused any change in catecholamine release from rabbit cortex and caudate nucleus or rat striatum. 20 references. (Author abstract modified)

003984 Rekhtman, M. B.; Samsonova, N. A.; Kryzhanovskiy, G. N. Institut obshchey patologii i patologicheskoy fiziologii AMN SSSR, Moskva, USSR **/The effect of diazepam on cyclic excitability changes in an epileptic focus in the cortex of the major hemispheres./** Vliyaniye diazepama na tsiklicheskoye izmeneniye vozbudimosti v epilepticheskom ochage kory bol'shikh polushariy. Neyrofiziologiya. 12(6):563-570, 1980.

Penicillin was applied to the motor cortex of rats, and n. ventroposterolateralis thalami was stimulated electrically at a rate of 1 per second at an intensity 3 times the threshold for the primary evoked potential, and the effect of diazepam on cyclic changes of excitability in an epileptic focus in the major hemispheres was studied. The application of penicillin and electrical stimulation produced an alternation of active and passive periods; during active periods epileptiform discharges appeared regularly at every electrical stimulus; during passive periods electrical stimulation of n. ventroposterolateralis thalami resulted in the emergence of evoked potentials only; injection of diazepam (2mg/kg) abolished rhythmogenesis in the epileptogenic focus, while 0.1mg/kg diazepam led to the disappearance of cyclic spike driving in the focus; and electrical stimulation of n. ventroposterolateralis thalami at a frequency of 2 per second restored cyclic spike driving. 18 references. (Journal abstract modified)

003985 Reubi, Jean-Claude; Perrin, Marilyn H.; Rivier, Jean E.; Vale, Wylie. Peptide Biology Laboratory, Salk Institute, P.O. Box 85800, San Diego, CA 92138 **High affinity binding sites for a somatostatin-28 analog in rat brain.** Life Sciences. 28(19):2191-2198, 1981.

Saturable and high affinity binding of an iodinated analog of a large and biologically active form of somatostatin, 125I(Leu8,D-Trp22,Tyr25)SS-28, was demonstrated in rat cortical membranes. Somatostatin, somatostatin-28, (D-Trp8)somatostatin, and (D-Trp22)somatostatin-28 completely displaced the radioligand in the nanomolar range. The inactive analog Des-Trp8-somatostatin and the unrelated peptide gonadotropin releasing hormone showed no affinity for these binding sites. Octapeptide and nonapeptide analogs of somatostatin were inactive. High binding was found in hippocampus, amygdala, tuberculum olfactorium, caudate/putamine, and cortex. Moderate binding was found in midbrain and hypothalamus, and no binding was seen in cerebellum. 29 references. (Author abstract modified)

003986 Richelson, Elliott. Dept. of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Tricyclic antidepressants and histamine H1 receptors.** Mayo Clinic Proceedings. 54:669-674, 1979.

Tricyclic antidepressants and some structurally related compounds were tested for their ability to antagonize histamine (H1) and muscarinic acetylcholine receptors of cultured mouse neuroblastoma cells. As a group, tertiary amine tricyclic antidepressants tended to be more potent than did secondary amine drugs at both receptors. The most potent antihistamine, doxepin hydrochloride, was about four times more potent than amitriptyline hydrochloride, about 800 times more potent than diphenhydramine hydrochloride, and about 8,000 times more potent than desipramine hydrochloride (the least potent tricyclic antidepressant at both the histamine (H1) and the muscarinic acetylcholine receptors). All tricyclic drugs except desipramine hydrochloride were more potent as antihistamines than as anticholinergics. It is concluded that doxepin hydrochloride and amitriptyline hydrochloride may be the most potent antihistamines known, and the antihistaminic potencies of these and the other tricyclic antidepressant drugs may relate directly to their ability to cause sedation and drowsiness in patients. 56 references. (Author abstract modified)

003987 Rittenhouse, Harry G.; Seguin, Edward B.; Fisher, Stephen K.; Agranoff, Bernard W. Agranoff: Neuroscience Lab., Mental Health Research Institute, University of Michigan, 1103 E. Huron, Ann Arbor, MI 48109 **Properties of a CDP-diglyceride hydrolase from guinea pig brain.** Journal of Neurochemistry. 36(3):991-999, 1981.

Enzymatic hydrolysis of the pyrophosphate bond of 5'-cytidine diphospho-1,2-diacyl-sn-glycerol (CDP-DG) was enriched in a lysosomal fraction of male guinea-pig cerebral cortex. When the purified enzyme was incubated with CDP dipalmitin, it produced stoichiometric amounts of CMP and phosphatidate. CDP-DG hydrolysis was not affected by the presence of excess amounts of CDP choline, CDP glycerol, sodium pyrophosphate, or cyclic AMP. 35 references. (Author abstract modified)

003988 Rodriguez, Sergia; Tamargo, Juan. Dept. of Pharmacology, Universidad Complutense, Madrid-3, Spain **Electrophysiological effects of imipramine on bovine ventricular muscle and Purkinje fibres.** British Journal of Pharmacology. 70(1):15-23, 1980.

The effects of imipramine (0.01mcM and 50 mcM) on bovine Purkinje fibers and ventricular muscle transmembrane potentials were examined. In electrically stimulated fibers, imipramine had no effect on resting membrane potential, but decreased the action potential amplitude, overshoot, and maximum rate of depolarization. In Purkinje fibers, imipramine decreased the conduction velocity and shifted the membrane responsiveness and recovery time curves downward and to the right. The properties of imipramine were quite similar to those of the class-1 antiarrhythmics quinidine and procainamide. 25 references. (Author abstract modified)

003989 Rosengarten, Helen; Friedhoff, Arnold J. Millhauser Laboratories, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Effect of prenatal neuroleptic treatment on membrane receptor development in the brain.** In: Parvez, H., Biogenic amines in development. New York, Elsevier/North Holland, 1980. (p. 607-616).

A review is presented of research into the effects of prenatal neuroleptic treatment on membrane receptor development in the rat and rabbit brain. Behavioral studies in animals treated with neuroleptics in the prenatal and early postnatal period demonstrate that catecholamine neurons are very vulnerable during ontogenesis, and that drugs administered during development of the dopaminergic system may induce alterations in transmitter functions, as evidenced in abnormal behavior. In histochemical studies, it has been found that maturation of the central noradrenergic system precedes that of the dopaminergic system. A number of drugs administered prenatally also have been found to have a detrimental effect on maze learning and conditioned avoidance performance. Further, differences in the rate of maturation of dopaminergic systems in different brain regions produce differences in vulnerability of those regions to early drug effects. Thus, substantial evidence exists that prenatal exposure to psychotropic agents, such as haloperidol, cannabis, triflupterazine, penfluridol, pimozide, clonidine, and chlorpromazine, can have substantial postpartum effects. 45 references.

003990 Ross, Stephen M.; Craig, Charles R. Craig: Dept. of Pharmacology and Toxicology, West Virginia University Medical Center, Morgantown, WV 26506 **Studies on gamma-aminobutyric acid transport in cobalt experimental epilepsy in the rat.** Journal of Neurochemistry. 36(3):1006-1011, 1981.

High and low affinity GABA transport were studied in crude brain homogenates and cerebral tissue slices from male Sprague-Dawley rats with cobalt metal implanted in the right and left cerebral cortices. High affinity GABA transport was reduced to 34% of control value 7 days after cobalt implantation, the time of peak seizure activity. Kinetic analysis of high affinity GABA transport revealed a significant decrease in maximal velocity 7 days after cobalt implantation; decrease was seen in the low affinity system. In vivo and in vitro administration of valproic acid had no effect on high or low affinity GABA transport. Results provide evidence for the involvement of GABA in experimental epilepsy. 18 references. (Author abstract modified)

003991 Ross, Svante B.; Hall, Hakan; Renyi, Anna L.; Westerlund, Douglas. Research and Development Laboratories, Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **Effects of zimelidine on serotoninergic and noradrenergic neurons after repeated administration in the rat.** Psychopharmacology. 72(3):219-225, 1981.

The antidepressant zimelidine inhibited the accumulation of 14C-5-hydroxytryptamine (14C-5-HT) and 3H-noradrenaline (3H-NA) in male Sprague-Dawley rat hypothalamic slices, and this effect was increased only slightly by prolonged oral treatment (5, 12.5 or 25mcmol/kg twice daily for 2 weeks). The accumulation of 5-HT was about four times more sensitive than that of NA to the inhibitory effects of acute or prolonged treatment with zimelidine. The inhibition of 5-HT accumulation was correlated significantly to plasma and hypothalamic concentrations of norzimelidine 14 hours after the last dose. The 5-HT concentration in whole blood was reduced markedly at the same doses that produced inhibition of 5-HT uptake in brain. The concentration of 5-hydroxyindoleacetic acid in whole brain was reduced after single or repeated administration of zimelidine, but the concentration of 5-HT was reduced only after prolonged treatment. The density of beta-adrenoceptors was reduced significantly by chronic administration of zimelidine, but 5-HT and dopamine receptor binding were not altered. 42 references. (Author abstract modified)

003992 Rouot, Bruno M.; U'Prichard, David C.; Snyder, Solomon H. Snyder: Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Multiple alpha2-noradrenergic receptor sites in rat brain: selective regulation of high-affinity (3H)clonidine binding by guanine nucleotides and divalent cations.** Journal of Neurochemistry. 34(2):374-384, 1980.

The selective regulation of high affinity (3H)clonidine binding to rat cortex alpha1-noradrenergic receptors by guanine nucleotides and divalent cations was investigated. Both kinetic and equilibrium experiments indicated the presence of distinct high and low affinity (3H)clonidine binding associated with alpha2-noradrenergic receptors in rat cerebral cortex membranes. Guanine nucleotides selectively decreased the numbers of high affinity (3H)clonidine binding sites, and had no influence on the low affinity sites. The influence of nucleotides was exerted by guanosine triphosphate, its nonmetabolized analogue, guanyl-5'-yl imidodiphosphate, and guanosine diphosphate, but not by guanosine 5'-monophosphate, adenosine diphosphate, adenosine triphosphate, and adenosine 5'-monophosphate. In contrast, divalent cations increased high affinity (3H)clonidine binding, an effect which was not evident at low affinity sites. Manganese was the most potent of the divalent cations, while magnesium and calcium were less active. Divalent cations and guanine nucleotides appeared to elicit interactive rather than simply additive influences upon alpha2-receptors. The inhibitory influence of sodium upon alpha2--eceptor binding of (3H)clonidine is exerted to the same extent upon both high affinity and low affinity (3H)clonidine binding. 32 references. (Author abstract modified)

003993 Ruth, Robin C.; Owens, Kenneth; Weglicki, William B. Dept. of Biophysics, P.O. Box 694, MCV Station, Richmond, VA 23298 **Inhibition of lysosomal lipases by chlorpromazine: a possible mechanisms of stabilization.** Journal of Pharmacology and Experimental Therapeutics. 212(3):361-367, 1980.

The mechanism of the stabilization of hepatic lysosomes from rats by chlorpromazine at pH 5.0 has been investigated. When lysosomes are incubated at 37 degrees C, pH 5.0, in O.25M sucrose, the latency of the lysosomal enzymes is gradually lost; this loss occurs more rapidly if the incubated lysosomes, particularly Triton filled lysosomes, are cooled before assay. Chlorpromazine protects maximally at a concentration of 0.0005M against the loss of latency which occurs at 37 degrees C, but, for Triton filled lysosomes, protection is much less if the incubated lysosomes are cooled before assay. Osmotic fragility curves were obtained by exposing lysosomes for short periods of time at pH 5.0 to buffers containing decreasing concentrations of sucrose. Rates of production of lysophospholipids and nonesterified fatty acids, as well as rates of degradation of triglycerides during incubation at 37 degrees C, pH 5.0 were examined. Chlorpromazine appeared to strongly inhibit endogenous phospholipase and triglyceride lipase activities. Although questions remain concerning the lack of protection when the incubated Triton filled lysosomes are cooled before assay, it is suggested that inhibition of the formation of potentially lytic lipid breakdown products is the basis of the stabilizing effect of the drug. 19 references. (Author abstract modified)

003994 Saratikov, A. S.; Alekseyeva, L. P.; Agarkova, V. P.; Zamoshchina, T. A. Kafedra farmakologii, Tomskiy meditsinskiy institut, Tomsk, USSR **/The effect of lithium hydroxybutyrate on the bioelectrical activity of the cortex and some subcortical structures of the rabbit brain./** Vliyaniye oksibutirata litiya na bioelektricheskuyu aktivnost' kory i nekotorykh podkorkovykh struktur mozga krolika. Farmakologiya i Toksikologiya. 43(4):353-356, 1980.

The effect of intravenous administration of lithium hydroxybutyrate (10mg/kg) on the bioelectrical activity of the cortex and subcortical structures of the rabbit brain was studied. Results show that: lithium hydroxybutyrate depressed the spontaneous bioelectrical activity of the cortex; this effect progressed to the subcortex; the drug reduced the electrical excitation of the motor cortex, caudate nucleus, thalamus, posterior hypothalamus, and midbrain reticular formation; it lowered the convulsive threshold of the amygdaloid complex; but it did not significantly alter hippocampal electrical excitability. These results show that the depressant effect of lithium hydroxybutyrate is comparable to that of lithium chloride. 15 references. (Journal abstract modified)

003995 Scatton, Bernard; Zivkovic, Branimir; Dedek, Jaroslav. Synthelabo-LERS, 31, Avenue Paul-Vaillant Couturier, F-92220 Bagneux, France **Antidopaminergic properties of yohimbine.** Journal of Pharmacology and Experimental Therapeutics. 215(2):494-499, 1980.

The effect of the alpha-adrenoceptor blocking agent yohimbine on cerebral dopamine metabolism was investigated in the rat. In both striatum and limbic areas, yohimbine increased: 1) homovanillic acid and dihydroxyphenylacetic acid levels; 2) tyrosine hydroxylase activity measured in vitro; 3) the in vivo accumulation of dihydroxyphenylalanine after NSD 1015; and 4) the rate of dopamine disappearance after alpha-methyl-p-tyrosine. These results suggest that alpha-adrenoceptors are not involved in the yohimbine-induced alteration of dopamine metabolism. It is concluded that yohimbine possesses postsynaptic dopamine receptor blocking properties in addition to its ability to inhibit alpha-adrenergic receptors. The failure of yohimbine to affect dopamine sensitive adenylate cyclase activity in striatal homogenates suggests an action of the compound on the D2 receptors. 48 references. (Author abstract modified)

003996 Schmidt, D. E.; Wecker, Lynn. Dept. of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232 **CNS effects of choline administration: evidence for temporal dependence.** Neuropharmacology. 20(6):535-539, 1981.

Choline (60mg/kg i.p.) attenuated the atropine-induced depletion of acetylcholine (ACh) in male Sprague-Dawley rat hippocampus and striatum, but this effect did not coincide with the occurrence of elevated free choline levels in brain. In the hippocampus, the effects of choline were not evident until 60 minutes after administration and persisted for at least 24 hours. The effects of choline in the striatum were evident immediately after administration, but lasted from less than 24 hours. Results suggest that exogenous choline administration increases the ability of cholinergic neurons to synthesize ACh in response to increased neuronal demand and that these effects are not mediated directly through increased total free brain choline or through increased steady-state levels of ACh. It is suggested that the use of specific pools of lipid bound choline plays a crucial role in central cholinergic mechanisms and may be responsible for the acute effects of choline on central cholinergic neurons. 21 references. (Author abstract modified)

003997 Schmucker, Douglas L.; Wang, Rose K. Cell Biology Section, V.A. Hospital, 4150 Clement St., San Francisco, CA 94121 **Effects of animal age and phenobarbital on rat liver glucose-6-phosphatase activity.** Experimental Gerontology. 15(1):7-13, 1980.

The effects of animal age and phenobarbital on rat liver glucose-6-phosphatase activity were investigated. Hepatic glucose-6-phosphatase activity declines gradually throughout development, maturation, and senescence in the Fischer 344 male rat. The loss of activity between maturity and senescence may be correlated with a concomitant reduction in the amount of hepatic smooth surfaced endoplasmic reticulum membrane (SER), a primary intracellular site of this enzyme. Phenobarbital, a repressor of glucose-6-phosphatase, caused a marked decline in the activity of this enzyme in young, mature, and senescent rats. However, the young animals exhibited a more rapid loss of enzyme activity and a quicker subsequent recovery to basal levels following the cessation of drug treatment than did either the mature or senescent rats. The data suggest that the hepatic adaptive capacity as manifested in enzyme repression and recovery declines as a function of animal age. This phenomenon may represent an additional biochemical index of chronological age, i.e., similar to the reported lag in hepatic enzyme induction with increasing age. 20 references. (Author abstract modified)

003998 Schwartz, Joan P. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **RNA polymerase II in C6 glioma cells: alpha-amanitin blockade of cyclic AMP phosphodiesterase induction by beta-adrenergic stimulation. (Unpublished paper).** Washington, DC, NIMH, 1981. 20p.

The role of RNA polymerase II, the enzyme responsible for the synthesis of messenger RNA (mRNA) in the induction of cAMP phosphodiesterase (cAMP PDE) in C6 glioma cells was examined in rat C6 glioma cells. Exposure of intact cells to isoproterenol, a beta-adrenergic receptor agonist, results in an increase in the activity of cAMP PDE. This increase in PDE activity is blocked by incubation of the cells with alpha-amanitin or actinomycin-D, suggesting that RNA polymerase II is necessary for synthesis of mRNA for the increase in PDE activity. The RNA polymerase II activity is not increased in isoproterenol-treated cells, although it is more strongly inhibited by alpha-amanitin. The Ki for the effect of alpha-amanitin on intact cells is 250nM, and the inhibitor acts rapidly, with a maximal effect within 15 minutes of exposure. The effect of alpha-amanitin is very specific as no change in various cytoplasmic or nuclear enzymes or metabolites was observed. 20 references. (Author abstract modified)

003999 Segawa, Tomio; Mizuta, Tadashi. Dept. of Pharmacology, Inst. of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **Effect of imipramine on central 5-hydroxytryptamine turnover and metabolism in rats.** Japanese Journal of Pharmacology. 30(6):789-793, 1980.

Levels of tritiated 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) were measured at various intervals after intraventricular injection of (3H)-5-HT to male Wistar rats treated acutely or chronically with imipramine or saline. Levels of (3H)-5-HT and (3H)-5-HIAA 2, 5, and 10 minutes after (3H)-5-HT injection were lower in rats given a single injection of imipramine than in controls, but these differences were not significant; at later times, values were higher in rats given a single injection of imipramine than in controls. In rats treated chronically with imipramine, levels of (3H)-5-HT and (3H)-5-HIAA were lower than control levels at all times after (3H)-5-HT injection. Endogenous levels of tryptophan and 5-HIAA were not altered by imipramine, but endogenous 5-HT content was decreased by long-term administration of imipramine. Results indicate that long-term treatment with imipramine accelerates the rate of disappearance of 5-HT from presynaptic neurons. 8 references. (Author abstract modified)

004000 Sharif, Najam A.; Roberts, Peter J. Roberts: Dept. of Physiology, School of Biochemical and Physiological Sciences, University of Southampton, Southampton, S09 3TU, England **L-aspartate binding sites in rat cerebellum: a comparison of the binding of L-(3H)aspartate and L-(3H)glutamate to synaptic membranes.** Brain Research. 211(2):293-303, 1981.

The binding of L-(3H)aspartate to sonicated, extensively washed, and preincubated cerebellar synaptic membranes from female Wistar rats was investigated. Binding was optimal under physiological pH and temperature conditions. The binding was saturable and appeared to involve a single population of binding sites. Quisqualate, 4-fluoroglutamate, and 2-amino-4-phosphonobutyrate, which are good displacers of (3H)glutamate binding, were only weakly active against the aspartate system. The proposed aspartate receptor preferring agonist N-methyl-D-aspartate was inactive. Monovalent cations reduced L-(3H)aspartate binding, while divalent cations enhanced binding. Freezing or cold storage of the membranes diminished (3H)aspartate binding, but lyophilization conferred substantial stability and markedly increased the affinity of the binding site. 24 references. (Author abstract modified)

004001 Shavit, Sara; Kutz, I.; Korczyn, A. D.; Gitter, S. Korczyn: Dept. of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel **Interactions between chlorpromazine and some of its metabolites.** Communications in Psychopharmacology. 4(6):495-500, 1980.

The interaction between chlorpromazine (CPZ) and four of its major metabolites, 7-hydroxy-CPZ, 8-hydroxy-CPZ, desmethyl-CPZ, and CPZ sulfoxide, was determined in experimental models of antipsychotic activity. None of the metabolites antagonized any of the CPZ effects. All of them had an additive effect to CPZ in reducing spontaneous motor activity. Prolongation of barbiturate sleeping time induced by CPZ and the abolition of amphetamine induced stereotyped behavior by CPZ were found to be potentiated by 7-hydroxy-CPZ, but not by the other metabolties. 9 references. (Author abstract)

004002 Shibla, Deborah B.; Gardell, Mary Ann; Neale, Joseph H. Dept. of Biology, Georgetown University, Washington, DC 20057 **The insensitivity of developing benzodiazepine receptors to chronic treatment with diazepam, GABA and muscimol in brain cell cultures.** Brain Research. 210(1-2):471-474, 1981.

The role of receptor ligands in the development of the benzodiazepine (BZ) receptor was studied in dissociated cell cultures prepared from fetal C57B1/6 mouse brain. A progressive increase in diazepam binding was observed during 3 weeks in culture, paralleling the development of these membrane receptors in vivo. The binding of neuronal and nonneuronal BZ receptor ligands indicated that nonneuronal elements may contribute more to total BZ receptor binding in culture than in adult brain in vivo. Chronic treatment with 1mcM diazepam, GABA, or muscimol for 3 weeks did not significantly alter BZ receptor binding in culture. Results indicate that the synthesis and catabolism of the BZ receptor are not regulated by long-term receptor occupancy. 8 references.

004003 Sibley, David R.; Creese, Ian. Creese: Dept. of Neurosciences M-008, University of California School of Medicine, San Diego, La Jolla, CA 92093 **Dopamine receptor binding in bovine intermediate lobe pituitary membranes.** Endocrinology. 107(5):1405-1409, 1980.

Evidence is presented that (3H)spiroperidol, or (3H)SPIRO and (3H)N-n-propylnorapomorphine, or (3H)NPA, a dopamine antagonist and agonist, respectively, bind stereospecifically to bovine intermediate lobe pituitary membranes. The specific binding was saturable and of high affinity. The rank order of catecholamines, phenothiazines, and related drugs in competing for (3H)SPIRO and (3H)NPA binding was consistent with interactions at a dopamine receptor. Guanine nucleotides selectively decreased agonist, but not antagonist, affinities for these binding sites. With the addition of 0.1 mM GTP, the ability agonists to displace (3H)SPIRO binding was decreased fivefold to sevenfold, while the dissociation constant for (3H)NPA was increased to 0.8 nM. These findings demonstrate dopamine receptors in the intermediate pituitary which may be involved in the regulation of beta-endorphin secretion. 27 references. (Journal abstract modified)

004004 Simpson, Lance L. Dept. of Pharmacology, College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York, NY 10032 **Evidence that there are subcellular pools of norepinephrine and that there is flux of norepinephrine between these pools.** Journal of Pharmacology and Experimental Therapeutics. 214(2):410-416, 1980.

Data are presented which suggest that norepinephrine (NE) exists in at least two subcellular pools, and models for NE storage in sympathetic nerves and for d-amphetamine-induced tachyphylaxis are described. D-Amphetamine evokes blood pressure responses that are dose dependent in magnitude and in shape. At a high dose, d-amphetamine evokes a response that decays biphasically. Chronic reserpine treatment diminishes the blood pressure response to a high dose of d-amphetamine, but it exerts a differential effect on the two components of the response. Acute reserpine treatment enhances blood pressure responses to d-amphetamine, mainly by enhancing the early, transient response. In addition, acutely administered reserpine reverses the tachyphylactic effect of d-amphetamine. 24 references. (Author abstract modified)

004005 Simpson, Lance L.; Barkai, Amiram. Dept. of Pharmacology, College of Physicians and Surgeons, 630 W. 168th St., New York, NY 10032 **Kinetic studies on the entry of d-amphetamine into the central nervous system: I. Cerebrospinal fluid.** Journal of Pharmacology and Experimental Therapeutics. 212(3):541-545, 1980.

The entry of d-amphetamine into the cerebrospinal fluid (CSF) following intravenous (i.v.) and intracerebroventricular (i.c.v.) administration was studied. After i.v. administration to rats, d-amphetamine undergoes a rapid distributive phase during which the drug is lost from plasma. The rate of entry into the CSF is also rapid, suggesting that the drug moves directly from plasma to CSF. Entry of drug into CSF is mainly by diffusion. Neither active transport associated with CSF formation nor active transport independent of CSF formation is quantatively important. After i.c.v. injection, d-amphetamine disappears from CSF relatively slowly. Egress of drug is mainly by diffusion, although active transport associated wit bulk absorption does play a measurable role. At steady-state, the concentration of free drug in plasma and in CSF is equivalent. 12 references. (Author abstract modified)

004006 Sjogren, C. AB Leo, Fack, S-251 00 Helsingborg, Sweden **The pharmacological profile of iofepramine, a new antidepressant drug.** Neuropharmacology. 19(12):1213-1214, 1980.

The pharmacological profile of lofepramine, a new antidepressant drug, is described. Lofepramine has a very low acute toxicity in experimental animals, has significantly lower effects than other antidepressants on salivary secretion, and has significantly lower effects than other antidepressants on blood pressure. In addition, lofepramine has significantly lower effects on heart beat than other antidepressants. Clinical studies have confirmed the slighter and less frequent side-effects of lofepramine and the equivalent therapeutic efficacy of lofepramine compared to other antidepressants. 4 references.

004007 Sloviter, Robert S.; Drust, Eugene G.; Damiano, Bruce P.; Connor, John D. Dept. of Pharmacology, Milton S. Hershey Medical Center, Penn State University College of Medicine, Hershey, PA 17033 **A common mechanism for lysergic acid, indolealkylamine and phenethylamine hallucinogens: serotonergic mediation of behavioral effects in rats.** Journal of Pharmacology and Experimental Therapeutics. 214(2):231-238, 1980.

A rat behavioral model that reflects central serotonin (5-HT) receptor activation in vivo was utilized in a study of indole and phenethylamine hallucinogens. Lysergic acid diethylamide (LSD) caused the 5-HT behavioral syndrome, and doses of LSD too low to cause the syndrome shifted the dose/response curve for 5-methoxy-N, N-dimethyltryptamine (a 5-HT receptor agonist) to the left. All indole and phenethylamine hallucinogens tested (5-methoxy-N,N-diethyltryptamine, ibogaine, mescaline, p-methoxyamphetamine, N,N-dimethyltryptamine, N,N-diethyltryptamine, and four other methoxy substituted amphetamines) evoked the same 5-HT behavioral syndrome in rats as did LSD. Studies on the mechanisms by which these compounds activated 5-HT receptors revealed that all except p-methoxyamphetamine were direct 5-HT agonists. P-Methoxyamphetamine produced its behavioral effect primarily through release of endogenous 5-HT. The findings support the hypothesis that lysergic acid, indoleaklylamine, and phenethylamine hallucinogens share a common mechanism of action, i.e., central 5-HT receptor activation. 59 references. (Author abstract modified)

004008 Smith, Charles B.; Garcia-Sevilla, Jesus A.; Hollingsworth, Peggie J. Dept. of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109 **Alpha2-adrenoreceptors in rat brain are decreased after long-term tricyclic antidepressant drug treatment.** Brain Research. 210(1-2):413-418, 1981.

The binding of 3H-clonidine to presynaptic alpha-adrenoreceptors to membranes isolated from the amygdala, hippocampus, anterior caudate nucleus, locus coeruleus, and hypothalamus of male Sprague-Dawley rats was decreased after 2 weeks of twice daily treatment with amitriptyline. Binding was not altered by antidepressant treatment for only 1 day. In vitro, a high concentration of amitriptyline caused a competitive inhibition of 3H-clonidine binding, but did not alter the number of binding sites after 2 weeks of amitriptyline may explain the subsensitivity of these receptors observed after prolonged administration of antidepressant drugs. Results suggest that endogenous depression may be the result of supersensitivity due to an increased number of presynaptic alpha2-adrenoreceptors in the brain. 17 references. (Author abstract modified)

004009 Smith, D. J.; Azzaro, A. J.; Zaldivar, S. B.; Palmer, S.; Lee, H. S. Dept. of Anesthesiology, West Virginia University Medical Center, Morgantown, WV 26506 **Properties of the optical isomers and metabolites of ketamine on the high affinity transport and catabolism of monoamines.** Neuropharmacology. 20(4):391-396, 1981.

The effect of racemic ketamine hydrochloride and its isomers and metabolites on high affinity transport of tritiated monoamine neurotransmitters was studied in a crude synaptosomal fraction from male Sprague-Dawley rat cerebral cortex. Each of the agents caused a concentration dependent inhibition of transport processes. The ()-isomer of ketamine was about four times more potent than (-)-ketamine was on catecholamine transport, but the (-)-isomer was slightly more effective against serotonin transport. An N-demethylated derivative of ketamine (metabolite-1) and a cyclohexanone derivative of metabolite-1 were weaker inhibitors than was the parent drug. Metabolite-1 was a competitive inhibitor and inhibited the oxidative deamination of monamines more effectively than did ketamine. 37 references. (Author abstract modified)

004010 Smith, John Robert. Oregon State University, Marine Science Center, Newport, OR **The effects of thyrotropin-releasing hormone on cyclic AMP accumulation in rabbit cerebral cortical tissue in the presence and absence of CNS depressants.** Life Sciences. 28(18):2065-2069, 1981.

The in vitro effects of thyrotropin releasing hormone (TRH) on cyclic AMP accumulation in cortical brain slices from rabbits is reported. Incubation of cortical tissue at three concentrations of TRH (1nM, 2nM, and 5nM) had no discernible effects on baseline cyclic AMP levels. When cortical tissue was incubated in the presence of pentobarbital or if cortical tissue was taken from animals pretreated with alpha-methyl-p-tyrosine (alpha-MPT), the baseline cyclic AMP accumulation was reduced. This decrease could be eliminated by the addition of TRH to the incubation media. When cortical tissue from atropine pretreated animals was used or when atropine was added to the incubation media, there was an increase in baseline cyclic AMP accumulation which was unaffected by the addition of TRH. These results show that TRH can modify cyclic AMP accumulation in mammalian cortical brain tissue but this ability may become evident only in situations where normal cyclic AMP concentration has been reduced. 15 references. (Author abstract)

004011 Soubrie, Philippe; Montastruc, Jean-Louis; Bourgoin, Sylvie; Reisine, Terry; Artaud, Francoise; Glowinski, Jacques. Glowinski: Groupe NB, INSERM U 114, College de France, 11, place Marcelin Berthelot, F-75231 Paris Cedex 5, France **In vivo evidence for GABAergic control of serotonin release in the cat substantia nigra.** European Journal of Pharmacology. 69(4):483-488, 1981.

Push/pull cannulae were used to estimate the release of endogenously synthesized 3H-serotonin in the substantia nigra (SN) and caudate nuclei (CN) of cats anesthetized with halothane. Unilateral nigral application of GABA reduced the local release of 3H-serotonin, whereas picrotoxin had the opposite effect. Both treatments failed to modify the 3H-serotonin release in the CN or contralateral SN. Results suggest that GABA neurons innervating the SN may regulate nigral serotonin transmission. The possibility that this regulation may be presynaptic or related to a change in the activity of the nigroraphe projection is discussed. 18 references. (Author abstract modified)

004012 Spealman, R. D.; Goldberg, S. R.; Kelleher, R. T.; Morse, W. H.; Goldberg, D. M.; Hakansson, C. G.; Nieforth, K. A.; Lazer, E. S. New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772 **Effects of norcocaine and some norcocaine derivatives on schedule-controlled behavior of pigeons and squirrel monkeys.** Journal of Pharmacology and Experimental Theraputics. 210(2):196-205, 1979.

The behavioral effects of norcocaine, three N-alkylated derivatives of norcocaine, and a phenyltropane analog of norcocaine (WIN 35,981) were compared with those of cocaine and a phenyltropane analog of cocaine (WIN 35,065-2). Squirrel monkeys and pigeons responded under a multiple fixed-interval, fixed-ratio schedule of food presentation; squirrel monkeys also responded under a multiple fixed-interval, fixed-ratio schedule of termination of a stimulus associated with electric shock. The effects of the drugs were qualitatively similar in each species, and depended mainly on the type of schedule that controlled responding. In the fixed-interval components, some doses of each drug increased responding; maximal increases in responding were similar with each drug. Each drug also altered the pattern of responding in the fixed-interval components; suitable doses increased the low rates of responding, which occurred early in the intervals, but decreased higher rates of responding, which occurred later in the intervals. In the fixed-ratio components, each drug decreased responding in a dose related manner, decreases resulted both from increased periods of pausing and from increased rates of responding once responding began. Neither N-allyl-norcocaine nor N-cyclopropykemethyl-norcocaine antagonized the rate decreasing effects of cocaine under a fixed-ratio schedule of food presentation. Norcocaine and its N-alkylated derivatives had the most rapid onset of effects and the shortest duration of effect followed in order by cocaine, WIN 35,981 and WIN 35,065-2. Comparative potency is noted. 33 references. (Author abstract modified)

004013 Speth, R. C.; Wastek, G. J.; Reisine, T. D.; Yamamura, H. I. Dept. of Pharmacology, University of Arizona School of Medicine, Tuczon, AZ 85721 **Benzodiazepine receptors: effect of**

tissue preincubation at 37 degrees C. Neuroscience Letters. 13:243-247, 1979.

(3H)Flunitrazepam binding to rat brain homogenates was assayed in incubations between zero and 37 degrees C and in incubations at zero degrees C. The affinity of brain benzodiazepine receptors for (3H)flunitrazepam was significantly greater in the samples incubated at temperatures above zero degrees C. There was no change in the number of benzodiazepine receptors. The possible mechanisms for this enhanced binding affinity and the methodological implications for this observation are discussed. (Journal abstract modified)

004014 Spindel, E.; Arnold, M. A.; Cusack, B.; Wurtman, R. J. Dept. of Nutrition and Food Science, Room 56-242, Massachusetts Institute of Technology, Cambridge, MA 02139 **Effects of caffeine on anterior pituitary and thyroid function in the rat.** Journal of Pharmacology and Experimental Therapeutics. 214(1):58-62, 1980.

Acute i.p. administration of caffeine lowered serum thyrotropin (TSH) and growth hormone (GH) levels in male Sprague-Dawley rats in a dose dependent manner, with median effective doses of 30 and 50mg/kg, respectively. TSH levels were depressed 1 to 6 hours after caffein injection and were correlated with serum caffeine levels greater than 20mcg/ml. The decrease in serum TSH was followed by decreases in serum 3, 3'5-triiodothyroxine and thyroxine 4 hours after caffeine injection. Theophylline and theobromine had effects similar to those of caffeine on hormone levels. Caffeine did not significantly affect hormone secretion when incubated directly with rat pituitaries in vitro. Administration of antisomatostatin antiserum to rats blocked the inhibitory effects of caffeine on serum GH levels, suggesting caffein inhibits GH and TSH secretion by releasing hypothalamic somatostatin. 35 references. (Author abstract modified)

004015 Sprick, U.; Oitzl, M.-S.; Ornstein, K.; Huston, J. P. Huston: Institute of Psychology III, University of Dusseldorf, Universitatsstrasse 1, 4000 Dusseldorf, West Germany **Spreading depression induced by microinjection of enkephalins into the hippocampus and neocortex.** Brain Research. 210(1-2):243-252, 1981.

Injections of leu-enkephalin, met-enkephalin, and D-ala2-met-enkephalinamide into the neocortex and hippocampus of male Sprague-Dawley rats elicited spreading depression (SD) in both structures. Naloxone pretreatment antagonized the enkephalin-induced hippocampal seizure activity that frequently preceded the wave of SD. Naloxone also prevented SD induced by leu-enkephalin in the neocortex and by met-enkephalin in the hippocampus, but did not alter SD induced by D-ala2-met-enkephalinamide in either structure. It is suggested that some reported behavioral effects of intracranial injections of enkephalins may be artifacts of hippocampal or cortical SD. 39 references. (Author abstract modified)

004016 Stabrovskiy, Ye. M.; Shpanskaya, L. S. Tsentral'naya nauchno-issledovatel'skaya laboratoriya, Institut usovershenstvovaniya vrachey im. S. M. Kirova, Leningrad, USSR **/The effect of pharmacological destruction of hypothalamic monoaminergic structures on body temperature and gas exchange during extreme cooling./** Effekt farmakologicheskoy destruktsii monoaminergicheskikh struktur gipotalamusa na temperaturu tela i gazoobmen pri ostrom okhlazhdenii. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova. 66(9):1307-1311, 1980.

The effect of pharmacological destruction of hypothalamic monoaminergic structures on body temperature and gas exchange during extreme cooling was studied in white male rats. The animals were divided into several groups, each of which was injected with various substances, some of which destroy the hypothalamic monoaminergic structures. Seven days after the injections the animals were placed for 1 hour in air temperatures of 22C and 5C. Gas exchange and body temperature were measured. Results show that pharmacological destruction of hypothalamic noradrenergic and dopaminergic terminals decreases body temperature, both in thermoneutral conditions and during cooling, by decreasing the heat production level. Destruction of hypothalamic serotoninergic terminals in conditions of extreme cooling lead to some hyperthermia by decreasing heat loss and increasing heat production. 6 references. (Journal abstract modified)

004017 Stanishevskaya, A. V.; Vekshina, N. L. Lab. psikhofarmakologii, Tsentral'nyy NII sudebnoy psikhiatrii imeni. V. P. Serbskogo, Moskva, USSR **/The role of opiate receptors of different brain regions in determining the emotional reactions of rats./** Rol' opiatnykh retseptorov razlichnykh otdelov mozga v formirovanii emotsional'nykh reaktsiy u krys. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova. 66(9):1287-1291, 1980.

The role of opiate receptors of different brain regions in determining emotional reactions was studied in male rats. Cannulas were implanted in the brain in the area of the amygdala and perioaqueductal gray matter. In some of the animals bipolar Nichrome electrodes also were implanted in the area of the lateral hypothalamus and periaqueductal gray matter. Morphine was introduced into the amygdala, causing emotional and behavioral changes characteristic of several forms of negative emotional states. Morphine also was introduced into the periaqueductal gray matter, causing inhibition of emotional reactivity. This was manifested in a reduction of sensitivity to positive and negative stimuli. Results show that the opiate receptors of rat amygdala and periaqueductal gray matter take part in the formation of different emotional states produced by local administration of morphine, with the nature of the states depending on the location of receptors in the cerebral structures. 14 references. (Journal abstract modified)

004018 Stoff, David M.; Gale, Karen. Adult Psychiatry Branch, NIMH, St. Elizabeths Hospital, WAW Building, Washington, DC 20032 **Beta-phenylethylamine reversal of chlorpromazine-induced activation of striatal tyrosine hydroxylase and catalepsy.** Brain Research. 211(2):492-496, 1981.

The ability of beta-phenylethylamine (PEA) to reverse the neurochemical and behavioral effects of striatal dopamine blockade was studied in male Sprague-Dawley rats. The stimulation of striatal tyrosine hydroxylase by 20mg/kg chlorpromazine was reduced by about 50% by a 75mg/kg dose of PEA and was reversed completely by 150mg/kg PEA. The 150mg/kg dose also partially reversed catalepsy induced by chlorpromazine. PEA was about 10 times less potent than amphetamine and 25 times less potent than apomorphine. 21 references. (Author abstract modified)

004019 Stramentinoli, G.; Catto, E.; Algeri, S. BioResearch Co., Research Laboratories, I-20060 Liscate, Milan, Italy **Decrease of noradrenaline O-methylation in rat brain induced by L-dopa. Reversal effect of S-adenosyl-L-methionine.** Journal of Pharmacy and Pharmacology. 32(6):430-431, 1980.

A 10mg/kg i.p. injection of L-dopa reduced brain concentrations of S-adenosyl-L-methionine (SAMe) and 3-methoxy-4-hydroxyphenylglycol-S04 (MHPG) in male CD-COBS rats. Intramuscular injection of 100mg/kg SAMe restored the concentration of MHPG to normal values and partially restored the SAMe concentration. Results indicate that exogenous SAMe can reverse the decreased O-methylation of brain noradrenaline induced by L-dopa and suggest that L-dopa-induced depletion of brain SAMe may affect methylation of other compounds that are substrates for methylating enzymes. 18 references.

004020 Study, Robert E. Laboratory of Neurophysiology, NINCDS, Building 36, Room 2C02, NIH, Bethesda, MD 20205 **Phenytoin inhibition of cyclic guanosine 3':5'-monophosphate (cGMP) accumulation in neuroblastoma cells by calcium channel blockade.** Journal of Pharmacology and Experimental Therapeutics. 215(3):575-581, 1980.

The mechanism of the phenytoin inhibition of cyclic GMP (cGMP) accumulation in neuroblastoma cells was investigated. It is noted that phenytoin inhibits the calcium dependent increases in cGMP produced by high potassium depolarization and by muscarinic receptor activation in N1E-115 neuroblastoma cells. The inhibition of the cGMP response to depolarization is half-maximal at 40mcM, similar to the plasma concentration associated with an optimal therapeutic response. The cGMP increase produced by the cationophore A23187 is insensitive to phenytoin blockade, indicating that the enzymatic machinery responsible for calcium stimulated cGMP accumulation is not affected. The calcium concentration/response curve for the cGMP response to high potassium showed noncompetitive inhibition by phenytoin. Results suggest that phenytoin inhibits cGMP responses by blocking calcium influx. The ability to block the depolarization-induced cGMP response is shared by other anticonvulsant which are effective against generalized tonic/clonic and cortical focal seizures but not by those effective against absence seizures. 50 references. (Author abstract modified)

004021 Subramanian, N.; Whitmore, W. L.; Seidler, F. J.; Slotkin, T. A. Slotkin: Box 3813, Duke University Medical Center, Durham, NC 27710 **Ontogeny of histaminergic neurotransmission in the rat brain: concomitant development of neuronal histamine, H-1 receptors, and H-1 receptor-mediated stimulation of phospholipid turnover.** Journal of Neurochemistry. 36(3):1137-1141, 1981.

The ontogeny of brain histaminergic transmission was studied in Sprague-Dawley rats. In the hypothalamus, which is rich in histaminergic innervation, histamine levels were low at birth, increased sharply at 8 days of age, and attained adult concentrations shortly thereafter. Regions poor in histaminergic innervation showed a high initial level of histamine and a subsequent decline with development. The developmental profile for H-1 receptor binding of 3H-mepyramine resembled that of the neuronal histamine pool; age related increases resulted from changes in the number of binding sites, with no change in affinity. The developmental profile for cellular responses to H-1 receptor activation was also similar to that observed for hypothalamic histamine levels. Results indicate that neuronal histamine, its key biosynthetic enzyme, and H-1 receptors coupled directly to cellular events develop simultaneously. 28 references. (Author abstract modified)

004022 Sugikawa, Masaki; Kagawa, Kyoichi; Tomizawa, Setsuo. Dept. of Pharmacology, Central Research Lab., Yomeishu Seizo Co., Ltd., 2132-37, Nakaminowa, Minowa-machi, Kami-Inagun, Nagano 399-46 Japan **Inhibitory action of the combination of aminopyrine and secobarbital on EEG activation, neocortical recruiting and augmenting responses in rabbits.** Japanese Journal of Pharmacology. 30(3):309-316, 1980.

The effect of aminopyrine and secobarbital (at a molar ratio of 2:1, the mixture and molecular compound) on rabbit EEG activation was examined. Secobarbital (40mg/kg, orally) elevated threshold voltages in the neocortical and hippocampal EEG produced by high frequency electrical stimulation of the midbrain reticular formation (MRF), nucleus centralis medialis (CM) of the thalamus, and posterior hypothalamus (PHA) by 40, 40, and 80%, respectively. Aminopyrine (80mg/kg) alone did not affect the arousal response. The molecular compound (120mg/kg) was more potent than secobarbital alone in inhibiting the arousal responses induced by stimulation of MRF and CM. The inhibitory action of the mixture (120mg/kg) on the PHA arousal response was significantly weaker than the effect of the molecular compound. Secobarbital and the molecular compound slightly inhibited the neocortical augmenting and recruiting responses. 10 references. (Author abstract modified)

004023 Supavilai, Porntip; Karobath, Manfred. Karobath: Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1090 Wien, Austria **In vitro modulation by avermectin B1a of the GABA/benzodiazepine receptor complex of rat cerebellum.** Journal of Neurochemistry. 36(3):798-803, 1981.

Avermectin-B1a (AVM), a macrolytic lactone anthelmintic agent, caused a concentration dependent increase in 3H-flunitrazepam binding to membranes from Sprague-Dawley rat cerebellum by increasing the affinity and number of binding sites. GABA, piperidine-4-sulfonic acid, and 4,5,6,7-tetrahydroisoxazolo(4,5,c)pyridine-3-ol diminished the effects of AVM on benzodiazepine receptor binding in a bicuculline sensitive fashion. The stimulation of 3H-flunitrazepam binding by AVM was also decreased by the pyrazolopyridines etazolate and catazolate. Results suggest that AVM, the pyrazolopyridines, and GABA modulate benzodiazepine receptor binding by acting at different but functionally related sites. 14 references. (Author abstract modified)

004024 Suzuki, O.; Katsumata, Y.; Oya, M. Dept. of Legal Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-31, Japan **Oxidation of beta-phenylethylamine by both types of monoamine oxidase: examination of enzymes in brain and liver mitochondria of eight species.** Journal of Neurochemistry. 36(3):1298-1301, 1981.

Beta-phenylethylamine (PEA) was characterized as a substrate for type-A and type-B monoamine oxidase (MAO) in brain and liver mitochondria of eight species. At 10.0mcM, PEA was almost specific for type-B MAO in all species. At 1000mcM, however, PEA was common for both types of MAO in rat brain and liver, human brain and liver, mouse brain, guinea-pig brain and liver, and bovine brain; at this concentration it was specific for type-B MAO in mouse liver, rabbit brain and liver, bovine liver, pig brain and liver, and chicken brain and liver. 25 references. (Author abstract modified)

004025 Sved, Alan F.; Goldberg, Irene M.; Fernstrom, John D. Fernstrom: Dept. of Nutrition and Food Science, Room 56-137, Massachusetts Institute of Technology, Cambridge, MA 02139 **Dietary protein intake influences the antihypertensive potency of methyldopa in spontaneously hypertensive rats.** Journal of Pharmacology and Experimental Therapeutics. 214(1):147-151, 1980.

When male spontaneously hypertensive Okamoto rats consumed a single meal before receiving methyldopa (MD), the increase in brain MD levels and the blood pressure reduction varied inversely with the meal's protein content. MD injection elicited a greater reduction in blood pressure and larger rise in brain MD in rats consuming a protein-free meal than in fasting animals and induced a smaller fall in blood pressure and a smaller increase in brain MD in rats ingesting a protein containing meal than in fasting animals. Ingestion of a food identical in amino acid content to 18% casein but containing an amino acid mixture instead of protein also blunted the MD-induced fall in blood pressure. However, consumption of a similar diet lacking the large neutral amino acids (LNAAS) but not other amino acid elicited an MD-induced blood pressure reduction similar to that caused by ingesting a protein free diet. The combined effects of meal consumption and MD injection on brain MD and blood pressure correlated significantly with the serum ratio of MD to the sum of the natural LNAAs and not with serum MD alone. Similar effects were observed with chronic dietary and MD treatments. Results indicate that dietary protein can significantly influence the potency of a clinically important amino acid drug that acts within the brain. 16 references. (Author abstract modified)

004026 Svensson, Torgny H. no address **Effect of chronic treatment with tricyclic antidepressant drugs on identified brain noradrenergic and serotonergic neurons.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):121-131, 1980.

The effect of chronic treatment with tricyclic antidepressant drugs on identified brain noradrenergic and serotonergic neurons was studied via single unit recording techniques. It is concluded that: 1) the feedback inhibition of central noradrenaline (NA) neurons in the dorsal raphe nucleus by some tricyclic drug (e.g. imipramine) is mediated by alpha-receptors of presynaptic character; 2) chronic treatment with imipramine, even in relatively high doses, causes a persistent inhibition of the activity of the NA neurons; 3) although some tricyclic antidepressasnt drugs may have presynaptic alpha-receptor blocking actions, others (e.g. chlorimipramine) obviously are devoid of such an effect; and 4) presynaptic serotonin receptors do not seem to show any altered response to a presynaptic serotonin receptor agonist. A panel discussion of these findings is appended. 36 references.

004027 Szeto, Hazel H.; Clapp, James F., III; Larrow, Rodney W.; Hewitt, Jean; Inturrisi, Charles E.; Mann, Leon I. Dept. of Pharmacology, Cornell University Medical College, New York, NY 10021 **Disposition of methadone in the ovine maternal-fetal unit.** Life Sciences. 28(19):2111-2117, 1981.

The distribution of methadone between mother and fetus after a single dose and at steady-state was determined, using the chronic pregnant ewe preparation. Following a single i.v. dose (O.5mg/kg) to the mother, methadone was rapidly distributed to the fetus; peak concentration in the umbilical vein occurred within 2 minutes. An umbilical venous/arterial gradient existed for 10 to 15 minutes after drug administration, indicating uptake of methadone by fetal tissues. Methadone concentration in the fetus was two to five times lower than those in the mother even in the postdistribution phase. When methadone was infused at a constant rate to the mother, steady-state was achieved in both mother and fetus within 4 to 5 hours. 11 references. (Author abstract modified)

004028 Takano, Yukio; Kohjimoto, Yoshiro; Kamiya, Hiro-o. Dept. of Pharmacology, School of Pharmaceutical Sciences, Fukuoka University, Fukuoka 814, Japan **The high affinity choline uptake system with respect to the muscarinic receptors using a synaptosomal fraction abundant in presynaptic membranes.** Japanese Journal of Pharmacology. 30(1):119-122, 1980.

The effects of atropine and oxotremorine on high affinity choline (Ch) uptake in guinea-pig brain were examined in vivo and in vitro. Ch uptake was significantly increased by i. p. administration of 5mg/kg atropine, but was not significantly decreased by oxotremorine (0.3mg/kg i.p.). In a synaptosomal fraction rich in presynaptic membranes, 10mcM and 100mcM atropine increased high affinity Ch by 51 and 56% respectively. A 10mcM concentration had no effect. Results suggest that high affinity Ch uptake is regulated by muscarinic receptors in presynaptic membranes. 18 references.

004029 Tardy, M.; Costa, M. F.; Rolland, B.; Fages, C.; Gonnard, P. Dept. de Biochimie, C.H.U. Henri-Mondor, F-94010 Creteil Cedex, France **Benzodiazepine receptors on primary cultures of mouse astrocytes.** Journal of Neurochemistry. 36(4):1587-1589, 1981.

Benzodiazepines were found to bind to glial membranes on a single type of site, with a high affinity on about 100 fmol of sites per mg protein. The number of binding sites is increased when the membranes are treated with Triton X-100. Antiepileptic drugs such as clonazepam and phenobarbital, and hypnotic drugs such as Ro-11-3128 and Ro-11-6896 are able in pharmacological concentrations to displace (3H)flunitrazepam from its glial binding sites. 13 references. (Author abstract)

004030 Taylor, John E.; Richelson, Elliott. Dept. of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Desensitization of histamine H1 receptor-mediated cyclic GMP formation in mouse neuroblastoma cells.** Molecular Pharmacology. 15:462-471, 1979.

Evidence is presented that histamine H1 receptor mediated cyclic GMP formation by intact mouse neuroblastoma cells (clone N1E-115) is attenuated by prolonged exposure to histamine. This desensitization was dependent upon the concentration of histamine and at 10mcM the half-time was about 9 min, whereas the half-time for resensitization in the absence of histamine was about 13 min. The order of potency for agonist-induced desensitization correlated with the order of potency for stimulating the H1 receptor in blocking desensitization by histamine. The ED50 for activation and for desensitization by histamine of the receptor mediated response was approximately equal to its KA for the H1 receptor. Omission of CA in the medium prevented cyclic GMP formation, but did not affect desensitization suggesting that cyclic GMP formation is not required for the development of the desensitized state. Desensitization was temperature dependent and marked inhibition of protein synthesis did not affect desensitization or its reversal. The ED50s for histamine stimulated cyclic GMP formation in control and in partially desensitized cells were similar, while the maximum response was reduced. 30 references. (Journal abstract modified)

004031 Taylor, W. J.; Wolf, A.; Young, J. M. Dept. of Pharmacology, University of Cambridge, Hills Road, Cambridge, CB2 2QD, England **The interaction of amine local anaesthetics with muscarinic receptors.** British Journal of Pharmacology. 71(1):327-335, 1980.

The binding of (-)-(3H)-quinuclidinyl benzilate (3H-QNB) to muscarinic receptors in crude synaptosomal preparations from guinea-pig brain was inhibited by the amine local anesthetics Proadifen, tetracaine, procaine, quinidine, procainamide, bupivacaine, lignocaine, and prilocaine, in decreasing order of potency. The concentration of tetracaine or prilocaine causing 50% inhibition of receptor specific binding of 3H-QNB varied linearly with the concentration of 3H-QNB, suggesting the interaction between these amines and the muscarinic receptor at lower concentrations of the amines is competitive. The log dose/response curve for the contractile response of longitudinal muscle strips from guinea-pig intestine to carbachol was shifted in a parallel fashion by low concentrations of tetracaine, but flattened by higher doses. A similar effect was observed for lignocaine and prilocaine. The curve for inhibition of 3H-QNB binding by carbachol was not significantly altered by 1mM prilocaine. Although prilocaine increases the affinity of nicotinic acetylcholine receptors for agonists, there was no evidence it has a similar effect on agonist binding to muscarinic receptors. 28 references. (Author abstract modified)

004032 Theodorou, A. E.; Hall, M. D.; Jenner, P.; Marsden, C. D. Marsden: University Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London SE5, England **Cation regulation differentiates specific binding of (3H)sulpiride and (3H)spiperone to**

rat striatal preparations. Journal of Pharmacy and Pharmacology. 32(6):441-444, 1980.

Female Wistar rat striatal membranes were used to compare the effects of monovalent and divalent cations on the binding of 3H-sulpiride, a substituted benzamide ligand for D-2 receptors, and 3H-spiperone, a typical neuroleptic that binds to both D-1 and D-2 receptors. The specific binding of 3H-sulpiride was highly dependent on the presence of sodium ions, whereas 3H-spiperone binding was not. Calcium, potassium, and magnesium ions did not markedly affect 3H-sulpiride binding. Results suggest that sodium dependency may account for the atypical properties of substituted benzamide drugs. 17 references.

004033 Theodorou, A.; Gommeren, W.; Clow, A.; Leysen, J.; Jenner, P.; Marsden, C. D. University Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London SE5, England **Chronic neuroleptic treatment specifically alters the number of dopamine receptors in rat brain.** Life Sciences. 28(14):1621-1627, 1981.

The specificity of the alteration of number of dopamine receptors in rat brain by chronic neuroleptic treatment was investigated. Trifluoperazine dihydrochloride was administered continuously to rats drinking water for 6 months. Animals killed at this time exhibited an increase in the number of dopamine receptors in the striatum and mesolimbic area, with a corresponding decrease in affinity for 3H-spiperone binding. However, no changes in the following were observed: 3H-apomorphine binding, 3H-dexetemide binding to muscarinic receptors, 3H-mepyramine binding to H1 histamine receptors, 3H-WB 4101 binding to alpha-noradrenergic receptors, and 3H-muscimol binding to GABA receptors. Thus, chronic neuroleptic administration to rats appears to alter specifically the number of cerebral dopamine receptors. 25 references. (Author abstract modified)

004034 Thornhill, J. A.; Cooper, K. E.; Veale, W. L. Division of Medical Physiology, Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada T2N 1N4 **Core temperature changes following administration of naloxone and naltrexone to rats exposed to hot and cold ambient temperatures. Evidence for the physiological role of endorphins in hot and cold acclimatization.** Journal of Pharmacy and Pharmacology. 32(6):427-430, 1980.

Core temperatures were measured in male Sprague-Dawley rats exposed to 4 or 38 degrees C and given a single subcutaneous 10mg/kg injection of naloxone or naltrexone. Both narcotic antagonists caused core temperature to decrease significantly below control level during exposure to cold and to increase above control level during exposure to heat. Results suggest that blockade of brain and pituitary endorphins by narcotic antagonists causes an acute disturbance in the animals' ability to acclimatize to severe changes in ambient temperature. 7 references.

004035 Ticku, Maharaj K. Dept. of Pharmacology, University of Texas Health Sciences Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **The effects of acute and chronic ethanol administration and its withdrawal on gamma-aminobutyric acid receptor binding in rat brain.** British Journal of Pharmacology. 70(3):403-410, 1980.

Acute treatment with ethanol (2 to 4mg/kg i.p.) increased the binding capacity of the low affinity GABA receptor site in male Sprague-Dawley rat brain. However, GABA receptor binding was not altered after chronic ethanol administration (1 to 21 days); this suggests that GABA receptors may adapt to the continuing presence of ethanol at the GABA synapse. The affinity of the low affinity GABA binding site 8 and 16 hours after withdrawal from chronic ethanol was significantly reduced, compared to the affinity in pair fed controls. Results suggest that GABA receptor sensitivity may play a role in some of the neuropharmacological effects of ethanol and in ethanol withdrawal symptoms. 41 references. (Author abstract modified)

004036 Ticku, Maharaj K. Dept. of Pharmacology, University of Texas Health Sciences Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Interaction of stereoisomers of barbiturates with (3H)alpha-dihydropicrotoxinin binding sites.** Brain Research. 211(1):127-133, 1981.

Racemic depressant barbiturates inhibited the binding of the GABA antagonist (3H)alpha-dihydropicrotoxinin ((3H)DHP) to male Sprague-Dawley rat brain membranes with median inhibitory concentrations ranging from 5 to 50mcM. The (-)-isomers of pentobarbital and secobarbital were three to four times more potent than their ()-isomers in inhibiting 3H-DHP binding, but the ()-isomer of hexobarbital was more potent than (-)-hexobarbital. The stereoisomers of 1-methyl-5-phenyl-propylbarbituric acid (MPPB), which show opposite pharmacological activity, inhibited (3H)DHP binding in a biphasic manner with a plateau at 4 to 100nM MPPB. The possibility that depressant and convulsant barbiturates act at the DHP site at the GABA synapse is discussed. 24 references. (Author abstract modified)

004037 Ticku, Maharaj K.; Burch, Troie. Division of Molecular Pharmacology, Dept. of Pharmacology, University of Texas Health Sciences Center, San Antonio, TX **Alterations in gamma-aminobutyric acid receptor sensitivity following acute and chronic ethanol treatments.** Journal of Neurochemistry. 34(2):417-423, 1980.

The effects of acute and chronic ethanol ingestion on the binding of the inhibitory neurotransmitter 3-H-gamma-aminobutyric acid (GABA) was investigated in inbred strains of mice. Acute effects were analyzed in DBA/2J (alcohol avoiding) and C57BL/6J (alcohol preferring) mice, while chronic effects were analyzed in C57 mice. Acute ethanol produced a significant increase in the binding capacity of the low affinity GABA binding site in both C57 and DBA mice, without significantly altering other binding parameters. The enhanced binding capacity may be responsible for the behavioral depression associated with ethanol use. Chronically treated C57 mice exhibited a decrease in the density of low affinity GABA receptor sites. The results suggest the possible involvement of GABA synaptic function in the neuropharmacological effects of ethanol. The possibility that chronic ethanol administration may result in adaptation of GABA receptors to the continuous presence of ethanol-induced CNS depression is discussed. 45 references. (Author abstract modified)

004038 Tortella, Frank C.; Moreton, J. Edward; Khazan, Naim. Moreton: Dept. of Pharmacology and Toxicology, Univ. of Maryland School of Pharmacy, 636 W. Lombard St., Baltimore, MD 21201 **Electroencephalographic and behavioral tolerance to and cross-tolerance between D-ala2-methionine-enkephalinamide and morphine in the rat.** Journal of Pharmacology and Experimental Therapeutics. 210(2):174-179, 1979.

Rats were given repeated i.vt. ijections of D-enkephalin (20mcg/4hr) or morphine (20mcg/4hr) for 72 to 96 hours during EEG recording. Initial epileptiform EEG and associated wet dog shakes occurred following D-enkephalin but not morphine. The epileptoid EEG progressed to a continuous high voltage EEG synchrony similar to morphine, and was associated with behavioral stupor. REM sleep also was suppressed. Repeated administration of D-enkephalin or morphine produced tolerance to their effects. When challenged with i.vt. morphine, D-enkephalin tolerant rats were cross-tolerant to morphine. Likewise, morphine tolerant rats were cross-tolerant to D-enkephalin. While the morphine tolerant rats demonstrated a marked abstinence syndrome when challenged with naloxone (10mg/kg, i.p.) no abstinence signs were observed in the D-enkephalin rats. The demonstration of tolerance and cross-tolerance between morphine and D-enkephalin suggests a similar mechanism of action, but the differential development of physical dependence may entail different mechanisms of receptor sensitivities for this effect. These findings of similarities and differences in the acute and chronic effects of D-enkephalin and morphine support the contention that heterogeneous opiate receptors may mediate their pharmacologic actions. 42 references. (Author abstract)

004039 Toth, Jeno; Lajtha, Abel. Center for Neurochemistry, Rockland Research Institute, Ward's Island, NY 10035 **Drug-induced changes in the composition of the cerebral free amino acid pool.** Neurochemical Research. 6(1):3-12, 1981.

The effects of insulin, hydroxybutyrate, deoxypyridoxine, chlorpromazine, codeine, morphine, puromycin, and cycloheximide on the composition of free amino acids in Swiss mouse and Wistar rat brain were tested. Signficant changes in a number of amino acids were seen with most compounds tested. The largest change was in alanine, which was increased 50% by glucose and decreased 20-60% by various drugs. Histidine levels were increased by many drugs, but nonessential amino acids were mostly decreased. The pattern of changes in mouse brain differed somewhat from that in rat brain. Results indicate that changes in amino acid levels may contribute to the pharmacological action of many drugs. 28 references. (Author abstract modified)

004040 Tramposch, A.; Sangdee, C.; Franz, D. N.; Karler, R.; Turkanis, S. A. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **Cannabinoid-induced enhancement and depression of cat monosynaptic reflexes.** Neuropharmacology. 20(6):617-621, 1981.

In a study of the mechanisms of the convulsant and anticonvulsant actions of delta9-tetrahydrocannabinol (THC) and cannabidiol (CBD), the effects of the cannabinoids were compared with those of phenytoin (PHT) on the spinal monosynaptic pathway of unanesthetized spinal cats. Small doses of THC enhanced pretetanic and posttetanic potentials, whereas PHT, CBD, and large doses of THC depressed the reflex. It is suggested that the excitatory influence on central synaptic transmission may contribute to the convulsant action of THC and that the depressant may account for the anticonvulsant action of cannabinoids. 25 references. (Author abstract modified)

004041 Trinus, K. F.; Skryma, R. N. Institut fiziologii im. A. A. Bogomol'tsa AN SSSR, Kiev, USSR **/The excitatory effect of atropine on the neurons of the frog sympathetic ganglia./** Vozbuzhdayuscheye deystviye atropina na neyrony simpaticheskikh gangliyev lyagushki. Neyrofiziologiya. 12(1):101-103, 1980.

Depolarization, accompanied by an increase in membrane conductance which was produced by atropine was studied in frog sympathetic ganglion neurons after activation of the receptors with different cholinomimetics. Results show that atropine perfusion caused excitatory effects if perfusion with acetylcholine or with a mixture of suberildicholine and 5-methylfurmethide had been performed beforehand, activating both nicotinic and muscarinic receptors. After activation of nicotinic receptors with suberildicholine, or muscarinic receptors with 5-methylfurmethide, atropine caused no changes in the electric properties of the membrane. These results suggest that atropine, acting on receptors which have been changed after the action of agonists, can evoke their activation. (Journal abstract modified)

004042 Trotta, E. E.; Freire, G. L. Depto. de Fisiologia, Instituto Biomedico, Universidade Federale Fluminense, Rua Hernani Mello no. 101, Niteroi, 24-210, RJ, Brazil **Inhibition by caffeine of calcium uptake by brain microsomal vesicles.** Journal of Pharmacy and Pharmacology. 32(11):791-793, 1980.

Caffeine inhibited the rate of calcium uptake and the steady-state level of calcium accumulation in rabbit brain microsomal vesicles. Calcium uptake was inhibited 16, 33, and 50% by 5, 10, and 15mM concentrations of caffeine, respectively. Similarities between the effects of caffeine on the calcium pump in brain and muscle are discussed. Results suggest the central stimulatory effects of caffeine may be due to inhibition of calcium uptake by subcellular vesicles and consequent facilitation of transmitter release. 21 references.

004043 Tskhadadze, L. V. Tbilisskiy gosudarstvennyy meditsinskiy institut, Tbilisi, USSR **/The effect of serotonin on the exosecretory action of the pancreas./** Vliyaniye serotonina na vneshnesekretornuyu deyatel'nost' podzheludochnoy zhelezy. Soobshcheniya Akademii Nauk Gruzinskoy SSR. 100(1):189-192, 1980.

The effect of serotonin on the exosecretory action of the dog pancreas was studied. Results show that: intramuscular administration of 0.1 to 1.0mg/kg of serotonin in adult dogs depresses the secretion of pancreatic juice, simultaneously reducing the alkalinity of the juice, and increasing diastase activity; serotonin strongly stimulated the secretion activity of the pancreas in puppies 3 to 4 months old. These results show that the action of serotonin on pancreatic secretion is caused by the excitation of the parasympathicus, since anticholinesterase substances increase the effect of serotonin. 10 references. (Journal abstract modified)

004044 Tucek, Stanislav; Dolezal, Vladimir; Sullivan, Ann C. Institute of Physiology, Czechoslovak Academy of Sciences, Videnska 1083, 14220 Prague, Czechoslovakia **Inhibition of the synthesis of acetylcholine in rat brain slices by (-)-hydroxycitrate and citrate.** Journal of Neurochemistry. 36(4):1331-1337, 1981.

The inhibition of synthesis of acetylcholine (ACh) in rat brain slices by (-)-hydroxycitrate and citrate is described. Slices of rat caudate nucleus were incubated in a solution of NaCl, KCl, MgCl2, NaH2PO4, NaHCO3, choline chloride, paraoxon, EGTA, and oxidizable substrates, and the inhibitory effects of (-)-hydroxycitrate and citrate on ACh synthesis were examined. The possibility is discussed that citrate alters the intracellular milieu in cholinergic neurons by chelating the intracellular Ca2 and decreases the supply of mitochondrial acetyl-CoA to the cytosol. The results with (-)-hydroxycitrate indicate that the cleavage of citrate by adenosine triphosphate citrate lyase is not responsible for the supply of more than about one third of the acetyl-CoA which is used for the synthesis of ACh when glucose or pyruvate are the main oxidizable substrates. This proportion may be even smaller, since (-)-hydroxycitrate possibly affects the synthesis of ACh from glucose and pyruvate by a mechanism similar to that of citrate, rather than by the inhibition of adenosine triphosphate citrate lyase. 29 references. (Author abstract modified)

004045 Vaynshteyn, G. B.; Pinegin, L. Ye. Lab. regulyatsii mozgovogo krovoobrashcheniya, Institut evolyutsionnoy fiziologii i biokhimii im. I. M. Sechenova, AN SSSR, Leningrad, USSR **/The dynamics of systemic venous, arterial, and cerebrospinal fluid pressure under i.v. administration of polyethylene glycol./** Dinamika tsentral'nogo venoznogo, arterial'nogo i likvornogo davleniy pri vvedenii polietilenglikolya. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova. 66(9):1369-1375, 1980.

The dynamics of systemic venous, arterial, and cerebrospinal fluid (CSF) pressure under i.v. administration of polyethylene glycol was studied in cats. Polyethylene glycol was administered i.v. to 12 anesthetized fully grown cats via the left femoral vein at the rate of 0.2ml/kg/min. Arterial pressure was measured with a mercury pressure gauge via a catheter in the right femoral artery; systemic venous pressure with a water pressure gauge via a catheter leading from the right femoral vein to the upper vena cava; and CSF pressure with a needle in the major occipital cistern, connected to a water pressure gauge. Results show that arterial pressure increased by 20 to 30mm Hg, and systemic venous pressure increased from 80 to 100mm H2O. Within 30 minutes of the end of polyethylene glycol administration the hemodynamics returned to initial levels due to increased diuresis, but cistern CSF pressure decreased as a result of dehydration of the brain. This decrease was counteracted by the high venous and arterial pressure, but after normalization of hemodynamics, the CSF pressure was decreased by 90 to 100mm H2O from the initial level. 15 references. (Journal abstract modified)

004046 Velasco, Francisco; Velasco, Marcos; Romo, Ranulfo. Div. of Neurophysiology, Dept. of Scientific Research, National Medical Center, IMSS, P.O. Box 73-032, Mexico City, Mexico **Specific and non-specific multiple unit activities during pentylenetetrazol seizures. I. Animals with isole'.** Electroencephalography and Clinical Neurophysiology. 49(5-6):600-607, 1980.

The sequence of activation and deactivation of multiple unit activities (MUA) in the brainstem reticular formation and pyramidal tract was studied in relation to clinical seizures and EEG and electromyographic (EMG) tonic/clonic discharges induced by pentylenetetrazol (PTZ) in cats immobilized by high spinal transection (encephale isole). Threshold doses of PTZ (20mg/kg i.v.) produced a significant increse in mesencephalic and pontine MUA 3 seconds after the termination of PTZ injection and anticipated for 5 seconds the onset of EEG tonic/clonic discharges. The mesencephalic and pontine reticular MUA and EMG MUA showed a further increase at the onset of EEG and pyramidal tract tonic/clonic discharges. EEG spike activity and pyramidal tract MUA decreased significantly 16 seconds later, whereas mescencephalic and pontine MUA and EMG remained high. Results suggest that PTZ-induced seizures start in the brinstem reticular formation and propagate to muscles by at least two pathways, pyramidal and extrapyramidal. Inhibition of seizure activity may start at the cortical level. 19 references.

004047 Wallis, David; Nash, Hywel. Dept. of Physiology, University College, P.O. Box 78, Cardiff CF1 1XL, Wales **Relative activities of substances related to 5-hydroxytryptamine as depolarizing agents of superior cervical ganglion cells.** European Journal of Pharmacology. 70(3):381-392, 1981.

Membrane potential changes evoked by 5-hydroxytryptamine (5-HT) and related substances were recorded by the sucrose gap method from rabbit ganglia superfused with Krebs solution at 20 degrees celsius. Some 5-HT analogues evoked prolonged responses distinctly different from the rapid depolarization and repolarization characteristic of 5-HT, while other analogues were inactive. Compounds dimethylated or trimethylated at the side chain nitrogen atom were also able to activate nicotinic receptors. The optimal requirements for activating ganglionic 5-HT receptors were a hydroxyl group at position 5 on the indole nucleus and a side chain bearing an ethylamine amino group. Methyl substituents around the terminal nitrogen were well tolerated, and a quaternary nitrogen could increase activity at the 5-HT receptor. Substitution of a methyl group at carbon atom 2 of the indole nucleus reduced activity. 34 references. (Author abstract modified)

004048 Warsh, Jerry J.; Godse, Damodar D.; Li, Peter P.; Cheung, Siu W. Sec. of Biochemical Psychiatry, Clarke Institute of Psychiatry, University of Toronto, 250 College St., Toronto, Ontario M5T 1R8, Canada **Postmortem stability of brain 3-methoxy-4-hydroxyphenylethyleneglycol and 3,4-dihydroxyphenylethyleneglycol in the rat and mouse.** Journal of Neurochemistry. 36(3):902-907, 1981.

Gas chromatography/mass fragmentography was used to study the postmortem stability of brain 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) and 3,4-dihydroxphenylethyleneglycol (DHPG) in male Wistar rats and male Swiss-Webster mice. Two hours after death, significant decreases were seen in rat brain free DHPG (20%), total MHPG (21%), and total DHPG (11%) at 4 degrees C; free MHPG increased significantly (50%). At 21 degrees, rat brain total MHPG increased (15%) 2 hours after death, but decreased (15%) at 4 and 8 hours; free MHPG levels were increased. Brain total and conjugated DHPG levels showed little change, but free DHPG levels were reduced at all times. In mouse brain, no significant changes in free MHPG and DHPG were seen within 24 hours at 4 degrees; at 21 degrees, mouse brain DHPG levels decreased and MHPG levels increased. 26 references. (Author abstract modified)

004049 Wastek, Gregory J.; Lopez, J. Rafael; Richelson, Elliott. Richelson: Dept. of Pharmacology, Mayo Foundation, Rochester, MN 55901 **Demonstration of a muscarinic receptor-mediated cyclic GMP-dependent hyperpolarization of the membrane potential of mouse neuroblastoma cells using (3H)tetraphenylphosphonium.** Molecular Pharmacology. 19(1):15-20, 1981.

The lipophilic cation (3H)tetraphenylphosphonium ((3H)TPP) was used to measure the transmembrane potential of cultured mouse neuroblastoma cells (clone N1E-115) in suspension. These cells accumulated approximately twice as much (3H)TPP in low K phosphate buffered saline (PBS) as they did in high K PBS. Accumulation in both cases was time and temperature dependent. Addition of carbachol significantly increased net (3H)TPP accumulation within 1 minute. Atropine, but not d-tubocurarine or pyrilamine, prevented the increase in (3H)TPP accumulation. The data suggest that muscarinic receptor responses in these cells may be mediated by a hyperpolarization of the cells' transmembrane potential subsequent to an increase in intracellular cyclic GMP. 28 references. (Author abstract modified)

004050 Watanabe, Yasuhiro; Itoh, Tadao; Yoshida, Hiroshi. Dept. of Pharmacology I, Osaka University School of Medicine, Nakanoshima, Kita-ku, Osaka 530, Japan **Developmental change of beta-adrenergic receptors in rat brain.** Japanese Journal of Pharmacology. 30(3):287-291, 1980.

Beta-adrenergic receptor binding was studied in the whole brain (minus cerebellum) of 2 and 6-day-old Sprague-Dawley rats. The maximal binding capacity and dissociation constant for (-)-3H-dihydroalprenolol (DHA) in the synaptic membrane fraction (SMF) did not vary with age. However, since the yield of SMF from the 2-day-old rat brain was lower than that from 6-day-old brain, the total number of binding sites was reduced in 2-day-old rats. The inhibitory effects of l-isoproterenol on DHA binding to the SMF was greater in 6-day-old animals than in 2-day-old animals. It is suggested that developmental changes in beta-adrenoceptors may alter the expression of catecholamine sensitive adenylate cyclase activity in rat brain during development. 14 references. (Author abstract modified)

004051 Watling, Keith J.; Dowling, John E. Watling: Biological Laboratories, Harvard University, Cambridge, MA 02138 **Dopaminergic mechanisms in the teleost retina. I. Dopamine-sensitive adenylate cyclase in homogenates of carp retina; effects of**

agonists, antagonists and ergots. Journal of Neurochemistry. 36(2):559-568, 1981.

A specific dopamine sensitive adenylate-cyclase was identified in homogenates of carp retina. Maximal stimulation by 100mcM dopamine produced a fivefold to tenfold increase in adenylate-cyclase; half maximal stimulation occurred at a concentration of 1mcM. Although l-noradrenaline and l-adrenaline both stimulated adenylate-cyclase activity, they were 10 times less potent than dopamine; l-phenylephrine and dl-isoprenaline were inactive. Apomorphine elicited partial stimulation, and various ergot alkaloids produced mixed agonist/antagonist responses. Dopamine stimulated adenylate-cyclase activity was potently antagonized by fluphenazine, alpha-flupenthixol, and alpha-piflutixol and to a lesser extent by haloperidol and spiperone. Metoclopramide, sulpiride, phentolamine, and propranolol did not antagonize the enzyme activity. The pharmacological profile of dopamine adenylate-cyclase in carp retina was similar to that for dopamine sensitive adenylate-cyclase in the mammalian CNS. 40 references. (Author abstract modified)

004052 Weiss, Benjamin; Prozialeck, Walter; Cimino, Mauro; Barnette, Mary Sellinger; Wallace, Thomas L. Dept. of Pharmacology, Medical College of Pennsylvania, Philadelphia, PA 19129 **Pharmacological regulation of calmodulin.** Annals of the New York Academy of Sciences. 356:319-345, 1980.

Evidence is reviewed that certain pharmacological agents can inhibit selectively the actions of calmodulin, the endogenous calcium binding protein that has been shown to regulate several biochemical and physiological processes. It is shown that this inhibition is caused by a selective calcium dependent binding of the drugs to calmodulin and that, of a large number of compounds studied, those having antispychotic activity display the hightest affinity for calmodulin. These studies suggest that many of the biochemical actions of these antipsychotics may be explained by a common mechanism: namely, selectively binding to and inhibiting the action of calmodulin. Preliminary results are presented from experiments which demonstrate that certain endogenous proteins, such as ACTH and beta-endorphin, that have been shown to alter behavior in animals also inhibit some actions of calmodulin. Overall, the results raise the possibility that calmodulin may be involved in behavioral processes, and that drugs known to alter behavior may produce their effects by interfering with the actions of calmodulin. 137 references.

004053 Wood, Paul L.; Stotland, M.; Richard, J. W.; Rackham, A. Dept. of Pharmacology, Merck Frosst Laboratories, C.P./P.O. Box 1005, Pointe Claire-Dorval, Quebec H9R 4P8 Canada **Actions of mu, kappa, sigma, delta and agonist/antagonist opiates on striatal dopaminergic function.** Journal of Pharmacology and Experimental Therapeutics. 215(3):697-703, 1980.

The development of a sensitive gas chromatographic/mass fragmentographic assay for simultaneous measurement of dihydroxyphenylacetic acid, homovanillic acid (HVA), dopamine (DA), and 3-methoxytyramine is described, and actions of specific opiate receptor agonists on dopaminergic function in the nigrostriatal pathway are discussed. In the rat, the mu-agonists morphine, etorphine, methadone, and phenazocine and the delta-agonist D-Ala2-D-Leu5 enkephalin all produced dose dependent elevations in the DA metabolites dihydroxyphenylacetic acid and HVA with no increase in 3-methoxytyramine. However, in the mouse, concomitant increases in HVA and 3-methoxytyramine were noted. The basis for this biochemical species difference in the coupling of intraneuronal metabolism and DA release remains to be determined. The epsilon-agonist, beta-endorphin, also elevated striatal dihydroxyphenylacetic acid and HVA indicating the possible coexistance of these receptors with mu-receptors and delta-receptors on nigrostriatal neurons. In contrast, experiments with the kappa-agonists ketazocine, ethylketazocine, and MR2034 indicate the absence of kappa-receptors on these neurons. Although the sigma-agonist SKF 10047 did alter DA metabolism, this action did not appear to involve opiate receptors. 60 references. (Author abstract modified)

004054 Woodman, O. L.; Rechtman, M. P.; Lang, W. J. Dept. of Pharmacology, University of Melbourne, Parkville, Victoria 3052, Australia **A comparison of the responses to some dopamine-receptor agonists and antagonists in the isolated perfused rat kidney.** Archives Internationales de Pharmacodynamie et de Therapie. 248(2):203-211, 1980.

Bromocriptine, 2,3,4,5-tetrahydro-7,8-dihydroxy-1-phenyl-1H-3-benzazepine (SK&F-38393), and apomorphine administered into Wistar rat kidneys perfused with physiological saline solution containing vasopressin and pretreated with an alpha-adrenoceptor antagonist produced vasodilator responses similar to those produced by dopamine. Responses to bromocriptine, SK&F-38393, and apomorphine were significantly reduced by the dopamine receptor antagonist ergometrine. Metoclopramide was an effective antagonist of dopamine, bromocriptine, SK&F-38393, and apomorphine. Apomorphine acted as a partial agonist on dopamine receptors in this preparation. Results are discussed in relation to the classification of dopamine receptor subtypes. 17 references. (Author abstract modified)

004055 Woodruff, G. N.; Freedman, S. B.; Poat, J. A. Dept. of Physiology and Pharmacology, University of Southampton, Bassett Crescent East, Southampton SO9 3TU, England **Why does sulpiride not block the effect of dopamine on the dopamine-sensitive adenylate cyclase?** Journal of Pharmacy and Pharmacology. 32(11):802-803, 1981.

The failure of sulpiride and domperidone to block the effect of dopamine on dopamine sensitive adenylate cyclase is discussed. It has been suggested that there are two types of dopamine receptors in the brain, a D1 receptor linked to adenylate cyclase and unaffected by sulpiride, and a D2 receptor blocked by sulpiride and not linked to adenylate cyclase. As an alternative explanation, it is suggested that the failure of sulpiride and domperidone to act as dopamine antagonists on adenylate cyclase may be due to their low lipid solubility and poor penetration into the brain. 14 references.

004056 Wu, P. H.; Phillis, J. W. Phillis: Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **The effect of noradrenaline on Na-K transport in rat cerebral cortical slices.** European Journal of Pharmacology. 69(4):529-531, 1981.

Noradrenaline (NA) increased the efflux of sodium (22Na) from cortical slices by 79% and increased the influx of potassium (42K) by 83%. These effects were not associated with changes in 22Na influx or 42K efflux and were not the result of increased exchange of these ions across the plasma membrane. The effects of NA on 22Na efflux and 42K influx were antagonized by ouabain or propranolol. Results indicate that NA stimulates the active coupled transport of Na and K across plasma membranes in rat cerebral cortical slices and support the proposal that NA hyperpolarizes central neurons by stimulating a membrane sodium pump. 5 references.

004057 Yamaguchi, Isamu; Kopin, Irwin J. Kopin: Laboratory of Clinical Science, Building 10, Room 2D-46, NIMH, Bethesda, MD 20205 **Differential inhibition of alpha-1 and alpha-2 adrenoceptor-mediated pressor responses in pithed rats.** Journal of Pharmacology and Experimental Therapeutics. 214(2):275-281, 1980.

The relative potencies of alpha-adrenoceptor antagonists at presynaptic and postsynaptic receptors were assessed by comparing their effects on increments in plasma norepinephrine levels and blood pressure during stimulation of the sympathetic outflow from the spinal cord of pithed rats. Since increments in blood pressure are related to the logarithms of increases in plasma norepinephrine, the latter appear to reflect levels of the catecholaine at vascular alpha-receptors. Phenoxybenzamine, dibenamine, and chlorpromazine were found to block preferentially postsynaptic alpha-receptors. Phentolamine and tolazoline were nearly equipotent at presynaptic and postsynaptic receptors; mianserin and piperoxan were more potent inhibitors of presynaptic alpha-receptors. Phenoxybenzamine and dibenamine were much more effective in blocking the pressor responses to sympathetic stimulation than administered norepinephrine. The opposite was true of mianserin and piperoxan, whereas phentolamine appeared to be about equipotent in blocking the pressor responses to stimulation and norepinephrine. Results suggest that the pressor effects of administered norepinephrine is mediated by different receptors (alpha2) than is the pressor response to stimulation of the sympathetic outflow, which appears to be mediated by alpha1 type adrenoceptors. 25 references. (Author abstract modified)

004058 Yeh, H. H.; Moises, H. C.; Waterhouse, B. D.; Woodward, D. J. Dept. of Cell Biology, University of Texas Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235 **Modulatory interactions between norepinephrine and taurine, beta-alanine, gamma-aminobutyric acid and muscimol applied iontophoretically to cerebellar Purkinje cells.** Neuropharmacology. 20(6):549-560, 1981.

Iontophoretically applied norepinephrine (NE) consistently enhanced the GABA-induced inhibition of cerebellar Purkinje cells in female Sprague-Dawley rats, but had minimal and inconsistent effects on Purkinje cell inhibition induced by taurine or beta-alanine. NE also enhanced Purkinje cell inhibitory responses induced by muscimol, an agent that binds to GABA receptors but is not an effective substrate for GABA uptake. Continuous application of GABA at low in iontophoretic currents did not augment Purkinje cell inhibition induced by superimposed GABA pulses. Since the facilitation of GABA inhibition by NE independent of GABA uptake or presynaptic transmitter release, the phenomenon appears to be postsynaptic. 41 references. (Author abstract modified)

004059 Yeroukalis, D.; Alevizos, B.; Gatzonis, S.; Stefanis, C. Dept. of Psychiatry, Athens University Medical School, Eginition Hospital, 74, Vass. Sophias Str., Athens, Greece **The effect of propranolol and its isomers on Purkinje neurones in rat cerebellum.** Neuropharmacology. 20(4):319-321, 1981.

The effect of dl-propranolol and its isomers on noradrenaline (NA) and serotonin (5-HT) responses of Purkinje neurons in rat cerebellum was studied. NA depressed firing of Purkinje neurons, and propranolol isomers failed to alter this depression. The inhibitory response to 5-HT was antagonized by dl-propranolol and l-propranolol, but not by d-propranolol. Results suggest that a postsynaptic 5-HT blocking effect rather than beta-adrenergic blocking activity may account for the clinical effects of propranolol in schizophrenic patients. 10 references. (Author abstract modified)

004060 Yokoi, Isao; Rose, Susan E.; Yanagihara, Takehiko. Yanagihara: Dept. of Neurology, Mayo Clinic, Rochester, MN **Benzodiazepine receptor: heterogeneity in rabbit brain.** Life Sciences. 28(14):1591-1595, 1981.

Binding characteristics of benzodiazepine receptors were studied with synaptosomal and microsomal membranes from rabbit brain in vitro utilizing (methyl-3H)diazepam. In synaptosomal membranes, both high and low affinity binding sites were identified with the dissociation constants (Kd) of 4.92 nM and 83.8 nM, respectively. However, only the high affinity site was identified with Kd of 3.96 nM with microsomal membranes. Benzodiazepine binding sites appear to include at least two subpopulations of receptors, one with high affinity and another with low affinity binding sites. 18 references. (Author abstract)

004061 Yonekawa, Wayne D.; Kupferberg, Harvey J.; Woodbury, Dixon M. Epilepsy Branch, Neurological Disorders Program, NINCDS, Bldg. 36, Rm. 5D-21, NIH, 9000 Rockville Pike, Bethesda, MD **Relationship between pentylenetetrazol-induced seizures and brain pentylenetetrazol levels in mice.** Journal of Pharmacology and Experimental Therapeutics. 214(3):589-593, 1980.

The relationship of the pentylenetetrazol (PTZ) induced seizure sequence of myoclonus, clonus, and hindlimb extension (TE) to brain PTZ levels was investigated, and the influence of route of administration on PTZ uptake and seizure development was examined. The critical brain PTZ level for onset of clonus ranged from 20mg/g to 50mg/g. Brain PTZ uptake was rapid after i.p. injection of PTZ. Uptake was slower after s.c. administration. TE onset did not appear to depend solely on brain PTZ levels since it sometimes occurred when brain PTZ levels were falling. Factors that could modulate the appearance of TE are discussed. 29 references. (Author abstract modified)

004062 Yoshizaki, Toshio; Tonda, Kanya. Shionogi Research Laboratories, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553, Japan **Effects of tricyclic antidepressants on tetrabenazine-induced depletion of brain monoamines in rats. 1. Norepinephrine.** Japanese Journal of Pharmacology. 30(5):721-729, 1980.

The effects of tricyclic antidepressants on the tetrabenazine (TB)-induced depletion of brain norepinephrine (NE) was studied in male Sprague-Dawley rats. Pretreatment with desmethylimipramine (DMI, 25 to 100mg/kg), imipramine (IM, 25 to 100mg/kg), chlorimipramine (100mg/kg), maprotyrine (50mg/kg), amitriptyrine (50 to 100mg/kg), chlorpromazine (CPZ, 5 to 20mg/kg), and amphetamine sulfate (10mg/kg) enhanced the NE depletion observed 2 hours after 2mg/kg TB. Reserpine-induced depletion of NE was enhanced only by amphetamine and was suppressed by DMI, IM, and CPZ. In rats pretreated with pargyline, TB produced a decrease in brain NE and an increase in normetanephrine. Results suggest that tricyclic antidepressants enhance TB-induced brain NE depletion by blocking NE reuptake from the synaptic cleft. 31 references. (Author abstract modified)

004063 Zimmermann, H.; Bokor, J. T. Abt. fur Neurochemie, MPI Biophys. Chemie, Gottingen, West Germany **5'-Triphosphate recycles independently of acetylcholine in cholinergic synaptic vesicles.** Neuroscience Letters. 13:319-324, 1979.

The effect of hemicholinium-3 (HC-3) on vesicular contents in acetylcholine (ACh) and 5-triphosphate (ATP) and the vesicular incorporation of 14C-label derived from (14C)choline and 3H-label derived from (3H)adenosine was examined after low frequency stimulation of the Torpedo electric organ. HC-3 caused an increased depletion of vesicular ACh and blocked the incorporation of 14C-label. Contents in vesicular ATP and 3H-incorporation were identical with and without HC-3. HC-3 blocked the recovery of electrical response of the tissue after stimulation but did not cause a change in vesicle numbers. Findings suggest that synaptic vesicles continue to recycle ATP in the absence of recycling of ACh and that vesicular uptake and storage of the two components are not coupled to each other. (Journal abstract modified)

004064 Zouhar, A.; Mares, P.; Brozek, G. Dept. of Neurology, Faculty of Medicine, Purkyne University, Brno, Czechoslovakia **Electrocorticographic activity elicited by metrazol during ontogenesis in rats.** Archives Internationales de Pharmacodynamie et de Therapie. 248(2):280-288, 1980.

Electrocorticographic changes induced by i.p. injections of metrazol were studied in developing male Wistar rats. The initial paroxysmal signs varied according to age. Discharges of waves in the alpha and theta range were seen in 4 to 7-day-old rats, whereas spikes in the frontal area were observed in 11 to 20-day-old rats. The typical mature reaction (theta waves in the occipital area) was seen in rats aged 24 days and older. In 4 and 5-day-old rats, generalized seizures were manifested as slow waves only. A shift toward fast frequencies was observed with development. A substantial part of this shift took place before day 14, after which bilateral synchrony of long lasting discharges was present also. 20 references. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

004065 Alander, T.; Grabowska-Anden, M.; Anden, N.-E. Anden: Dept. of Medical Pharmacology, Box 573, Biomedicum, S-751 23 Uppsala, Sweden **Physiological significance of dopamine autoreceptors as studied following their selective blockade by molindone.** Journal of Pharmacy and Pharmacology. 32(11):780-782, 1980.

Molindone was about four times more potent in blocking the presynaptic effects of apomorphine than in blocking its postsynaptic effects in male Sprague-Dawley rats. Molindone inhibited the effects of apomorphine on dopamine synthesis in a dose as low as 0.45mg/kg, but antagonized the effect of apomorphine on rotation only at doses of 2.75mg/kg or higher. Results are discussed in relation to the physiological role of dopamine autoreceptors. 13 references.

004066 Arnt, Jorn. H. Lundback and Co. A/S, Dept. of Pharmacology and Toxicology, Ottiliavej 7-9, DK-2500 Valby, Denmark **Hyperactivity following injection of a glutamate agonist and 6,7-ADTN into rat nucleus accumbens and its inhibition by THIP.** Life Sciences. 28(14):1597-1603, 1981.

The potent glutamate receptor agonist (R,S)-alpha-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) was found to induce a dose related hyperactivity after bilateral injection of 0.025 to 0.5mcg into rat nucleus accumbens. The dopamine agonist 6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (6,7-ADTN) induced a similar effect. The hyperactivity induced by AMPA and 6,7-ADTN was antagonized by cis-Z-flupentixol. Reserpine plus alpha-methyltyrosine inhibited AMPA but not 6,7-ADTN-induced motility. Furthermore, AMPA and 6,7-ADTN-induced motility was antagonized by the GABA agonist THIP after systemic administration and intraaccumbens injection. Results suggest that glutamatergic mechanisms are important in regulation of locomotor activity by influencing mechanisms afferent to dopamine receptors. Both glutamate and dopamine systems are under inhibitory GABAergic control. 27 references. (Author abstract modified)

004067 Arushanyan, E. B.; Shishlyannikova, L. V. Kafedra farmakologii, Chitinskiy meditsinskiy institut, Chita, USSR **/The effect of small doses of haloperidol and clozapine on behavioral shifts in cats, arising after cessation of electrical stimulation of the caudate nucleus./** Vliyaniye malykh doz galoperidola i klozapina na povedencheskiye sdvigi u koshek, voznikayushchiye posle prekrashcheniya elektricheskoy stimulyatsii khvostatogo yadra. Farmakologiya i Toksikologiya. 43(4):364-368, 1980.

The effect of small doses of haloperidol and clozapine on behavioral shifts occurring after cessation of repeated low frequency electrical stimulation of the caudate nucleus head was studied in cats. Results show that haloperidol (0.03 to 0.06mg/kg) and clozapine (0.25mg/kg) facilitated the development of such behavioral shifts, and potentiated this effect. These results show that triggering of tonic inhibitory effects of the nucleus by means of neuroleptics can affect not only motor activity but also mental processes. 13 references. (Journal abstract modified)

004068 Ayvazashvili, I. M.; Iordanishvili, G. S.; Nikolaishvili, M. I. no address **/The effect of p-chlorophenylalanine on the distribution of biogenic amines in the brain, and on memory in rats./** Vliyaniye parakhlorfenilalanina na raspredeleniye biogennykh aminov v golovnom mozge i na pamyat' u krys. Soobshcheniya Akademii Nauk Gruzinskoy SSR. 100(1):185-188, 1980.

The effect of parachlorphenylalanine on the distribution of biogenic amines in the brain, and on memory was studied in rats. Results show that: the biochemical changes caused by parachlorphenylalanine, such as the decrease in the ratio of noradrenaline to serotonin in the anterior regions of the cerebral hemispheres and in the hippocampus, altered different types of memory; these changes facilitated the formation and maintenance of an emotional reaction of fear, suppressed the formation and manifestation of conditioned defense behavior, but had no effect on the reproduction and performance of previously elaborated and consolidated defense behavior. 7 references. (Journal abstract modified)

004069 Bell, Graham A.; Morgan, Ian G. Dept. of Behavioural Biology, Research School of Biological Sciences, Australian National University, Canberra ACT 2601, Australia **The effects of colchicine and vinblastine on memory in chicks.** Behavioural Brain Research. 2(3):301-322, 1981.

Colchicine, injected bilaterally into the forebrain of day old chicks at times before and after one trial avoidance learning, was found to produce transient amnesia for one to three hours after learning, that could not be accounted for as a perceptual or attentional defect. The amnesia was dose dependent and was produced only when injections occurred within a limited period before and after learning. Control birds injected with saline of lumicolchicine, a biologically inactive derivative of colchicine, showed normal retention. Vinblastine sulphate, which also interrupts microtubular networks and hence axonal flow, had no amnesic properties. During the amnesic period, there was no evidence of gross perturbation of brain function. It is suggested that the amnesic episode represents destruction of one of the stages of a multiple independent parallel process of memory consolidation. 50 references. (Author abstract modified)

004070 Beninger, Richard J.; Mason, Stephen T.; Phillips, Anthony G.; Fibiger, Hans C. Dept. of Psychology, University of British Columbia, Vancouver, BC, Canada V6T 1Y7 **The use of conditioned suppression to evaluate the nature of neuroleptic-induced avoidance deficits.** Journal of Pharmacology and Experimental Therapeutics. 213(3):623-627, 1980.

The effects of pimozide were studied in male Wistar rats given one way avoidance training in which each trial was initiated by a 10 second tone stimulus and terminated by a shuttle response during the tone (avoidance) or by a response during electric shock (escape). Rats treated with 0.5 or 1.0mg/kg i.p. pimozide failed to acquire the avoidance response, but escaped readily when shock was presented. The same rats were then given several sessions of food reinforced lever-pressing in a different apparatus with no drug treatment. Responding in this model decreased significantly when the tone that had signalled shock in the avoidance sessions was presented for a 1 minute period. This finding indicates that the pimozide treated rats had learned the asociation between the tone and shock, even though they had failed to acquire the avoidance response in the shuttlebox. It is suggested that the neuroleptic treated animals failed to avoid because of a deficit in the ability to initiate responses rather than a deficit in associative learning. 28 references. (Author abstract modified)

004071 Bergman, Jack; Johanson, Chris E. Johanson: Dept. of Psychiatry, University of Chicago, Pritzker School of Medicine, 950 East 59th St., Chicago, IL **The effects of electric shock on responding maintained by cocaine in rhesus monkeys.** Pharmacology Biochemistry and Behavior. 14(3):423-426, 1981.

The effect of electric shock was studied in three rhesus monkeys self-administering cocaine (100mcg/kg/infusion) under a fixed-ratio 10 schedule of drug delivery. Delivery of electric shock at intermediate intensity levels at the start of each infusion initially reduced cocaine maintained responding. Adaptation to the punishing effect of shock occurred within five test sessions in each monkey. Adaption did not occur at higher intensity levels that completely eliminated concaine maintained responding. 18 references. (Author abstract modified)

004072 Bhargava, H. N. Dept. of Pharmacognosy and Pharmacology, University of Illinois, Medical Center, Chicago, IL 60680 **The effects of peptides on tolerance to the cataleptic and hypothermic effects of morphine in the rat.** Neuropharmacology. 20(4):385-390, 1981.

Administration of melanotropin release inhibiting factor or its cyclic analogue, cyclo(Leu-Gly), prior to and during morphine pellet implantation inhibited the development of tolerance to the cataleptic and hypothermic effects of morphine in male Sprague-dawley rats. Previous studies have show that these peptides also inhibit tolerance to the analgesic effects of morphine. It is suggested that tolerance to the cataleptic, analgesic, and hypothermic actions of morphine may involve a common mechanism, possibly changes in dopamine receptor supersensitivity. 28 references. (Author abstract modified)

004073 Bittner, Stephen E.; Wagner, George C.; Aigner, Thomas G.; Seiden, Lewis S. Seiden: Dept. of Pharmacology and Physiology, University of Chicago, 947 E. 58th St., Chicago, IL 60637 **Effects of a high-dose treatment of methamphetamine on caudate dopamine and anorexia in rats.** Pharmacology Biochemistry and Behavior. 14(4):481-486, 1981.

The effects of d-methamphetamine (MA) on the intake of sweetened condensed milk by male Sprague-Dawley rats were determined before and after treatment with 50mg/kg MA or saline twice daily for 4 days. Animals that were more sensitive to the anorexic effect of MA prior to the high dose treatment were more sensitive to the lethal effects of the high dose treatment. This treatment decreased brain dopamine for 6 months, but did not alter the anorexic or stereotypic behavior elicited by MA. Daily administration of 2.5mg/kg MA 15 minutes before presentation of milk produced tolerance to the drug's anorexic effect in both control and high dose treatment groups. After 4 to 5 weeks of repeated administration of 2.5mg/kg MA milk intake and bodyweight were higher in the control group than in treated rats. 14 references. (Author abstract modified)

004074 Bodnar, Richard J.; Merrigan, Kevin P.; Wallace, Margaret M. Dept. of Psychology, Queens College, CUNY, Flushing, NY 11367 **Analgesia following intraventricular administration of 2-deoxy-D-glucose.** Pharmacology Biochemistry and Behavior. 14(4):579-581, 1981.

Flinch/jump thresholds were studied in male Sprague-Dawley rats 30, 90, and 180 minutes after intraventricular injections of 3.5, 5.0, and 10.0mg/kg 2-deoxy-D-glucose (2-DG) and systemic injections of 350 or 500mg/kg 2-DG. Intraventricular 2-DG injections increased jump thresholds for up to 180 minutes across all test doses. Flinch thresholds also increased, but in a manner dissociated from jump thresholds. Animals with cannulae located near but not in the lateral ventricle displayed delayed analgesic effects. The magnitude of intraventricular 2-DG analgesia was not as great as that of the higher dose systemic injections. 15 references. (Author abstract modified)

004075 Borodkin, Yu. S.; Lapina, I. A.; Bul'on, V. V.; Hartmann, G.; Hahn, J.; Lissak, K. Lab. eksperimental'noy farmakologii, Otdel farmakologii, Institut eksperimental'noy meditsiny AMN SSSR, Leningrad, USSR **/The effect of propylnorantifein on behavioral reactions, adrenocortical activity, and energy metabolism in the animal brain./** Povedencheskiye reaktsii, adrenokortikal'naya aktivnost' i energeticheskiy obmen golovnogo mozga zhivotnykh pri deystvii propilnorantifeina. Farmakologiya i Toksikologiya. 43(4):356-360, 1980.

The effect of propylnorantifein on behavioral reactions, adrenocortical activity and energy metabolism in the rat brain was studied biochemically and by open-field, passive-avoidance, and self-stimulation of the medial bundle of the forebrain and raphe. Results show that: propylnorantifein (5mg/kg) decreased self-stimulation, changed the emotional memory in response to pain stimulation, and increased the concentration of corticosteroids in blood plasma; and for 3 hours after administration there was a reduced amount of glycogen in the brain tissue, and an increased level of creatine phosphate. Results also show that the blockade of alpha-adrenoceptors and beta-adrenoceptors, in particular, drastically reduced the action of the drug. These results suggest that propylnorantifein may activate the adenylate cyclase system in brain tissue. 8 references. (Journal abstract modified)

004076 Botticelli, Lawrence J.; Wurtman, Richard J. Wurtman: Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Sciences, MIT, Cambridge, MA 02139 **Choline reverses naloxone-induced decreases in hippocampal acetylcholine content and suppresses escape behavior in opiate-dependent rats.** Brain Research. 210(1-2):479-484, 1981.

The effects of exogenous choline (Ch) on naloxone precipitated opiate withdrawal were studied in male Sprague-Dawley rats. In morphine dependent rats, naloxone administration significantly decreased hippocampal acetylcholine (ACh) content. This ACh decrease was blocked by pretreatment with Ch. Ch also decreased the severity of the opiate abstinence syndrome: the median effective dose of naloxone required to precipitate escape behavior in morphine dependent rats was tripled by Ch pretreatment. Results suggest that by accelerating ACh synthesis, Ch increases presynaptic stores of ACh and sustains ACh release after opiate withdrawal. 26 references.

004077 Brady, Linda S.; Holtzman, Stephen G. Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Locomotor activity in morphine-dependent and post-dependent rats.** Pharmacology Biochemistry and Behavior. 14(3):361-370, 1981.

The effects of morphine and naloxone on the locomotor activity of morphine dependent, nondependent, and postdependent male CFE rats were tested. Locomotor activity of dependent and nondependent rats was increased by low doses of morphine and reduced by higher doses; both effects were antagonized by naloxone. Chronic morphine treatment produced marked tolerance to the depressant effect of high morphine doses, but not to the stimulant effect of low doses. Postdependent animals remained tolerant to the depressant effect of high doses of morphine. The development of tolerance to the depressant but not the stimulant effect of morphine in dependent and nondependent animals suggests that different neuronal substrates mediate morphine-induced stimulation and depression of locomotor activity. Abrupt or naloxone precipitated withdrawal generally disrupted locomotor activity in dependent rats. Naloxone also decreased activity in postdependent animals. Thus, chronic morphine administration produced long-lasting changes in the sensitivity of dependent and postdependent rats to the effects of morphine and naloxone on locomotor activity. 22 references. (Author abstract modified)

004078 Brown, Janet; Handley, Sheila L. Handley: Pharmacological Laboratories, Dept. of Pharmacy, University of Aston, Birmingham B4 7ET, England **Effects on the pinna reflex of drugs acting at alpha-adrenoceptors.** Journal of Pharmacy and Pharmacology. 32(6):436-437, 1980.

The effects of alpha-adrenoceptor agonists and antagonists on the pinna reflex (head shaking in response to ear stimulation) were studied in male TO mice. The alpha2-adrenoceptor agonist clonidine, guanfacin, and guanabenz inhibited the pinna reflex in a dose dependent manner, but the alpha1-adrenoceptor agonists methoxamine and oxymetazoline were ineffective after subcutaneous administration. The inhibitory affects of the alpha2-adrenoceptor agonists were antagonized by the alpha2-adrenoceptor antagonists yohimbine and piperoxane, but not by the alpha1-adrenoceptor antagonist prazocin. 12 references.

004079 Cappeliez, P.; White, N. White: Dept. of Psychology, McGill University, 1205 Dr. Penfield Avenue, Montreal, Quebec, Canada **Lithium induces dose-related increases and decreases in activity levels in the rat.** Psychopharmacology. 73(1):34-38, 1981.

The effect of intraperitoneal lithium chloride on the activity levels of rats was measured by counting photocell interruptions in an open-field. Treatment with 0.15mEq/kg increased activity and 1.5mEq/kg decreased activity. In a second experiment, behavioral observations were added to the photocell counts of open-field activity, and the increase observed with 0.15mEq/kg LiCl in Experiment 1 was compared with the increase in open-field activity produced by 0.4g/kg ethanol. The two drugs produced similar increases in cell counts and walking, and similar decreases in sitting and sniffing. Lithium produced significantly more rearing and behavior directed at the cage than did ethanol. Following Johnson's hypothesis of lithium action, these findings are discussed in the context of lithium-induced changes in responsiveness to the environment. It is suggested that, at 0.15mEq/kg, lithium chloride might increase reactivity to the environment. 37 references. (Author abstract)

004080 Carey, Michael P.; Ross, John A.; Enns, Melvin P. Enns: Dept. of Psychology, St. Lawrence University, Canton, NY 13617 **Naloxone suppresses feeding and drinking but not wheel running in rats.** Pharmacology Biochemistry and Behavior. 14(4):569-571, 1981.

The effects of naloxone hydrochloride on wheel running and food and water intake were studied in male Long-Evans rats. The 3 hour food and water intake of nondeprived rats was suppressed by 10mg/kg naloxone but not by 1mg/kg. Neither dose of naloxone altered the number of wheel revolutions in food deprived or nondeprived animals. Results indicate that the suppressive effects of naloxone are specific to feeding and drinking. 14 references. (Author abstract modified)

004081 Carli, Giancarlo; Farabollini, Francesca; Fontani, Giuliano. Istituto di Fisiologia Umana, Universita di Siena, Via Laterina 8, I-53100 Siena, Italy **Effects of pain, morphine and naloxone on the duration of animal hypnosis.** Behavioural Brain Research. 2(3):373-385, 1981.

The effects of pain, morphine, and naloxone on the duration of animal hypnosis (tonic immobility) were investigated in rabbits. Long lasting irritative pain, produced within 15 minutes of formalin injection, potentiated the duration of hypnosis. Morphine, in the absence of painful stimuli, also potentiated hypnosis duration, and this effect was antagonized by naloxone. Naloxone reduced hypnosis duration, but only at high doses (15mg/kg). In a condition of irritative pain, the potentiation of hypnosis duration was abolished by naloxone (5mg/kg). Hypnosis response was abolished in six out of seven morphine tolerant rabbits, but prolonged pain restored the response. The hypothesis that an opioid mechanism may be activated during animal hypnosis is discussed. 63 references. (Author abstract modified)

004082 Caruso, Thomas P.; Larson, Dennis L.; Portoghese, P. S.; Takemori, A. E. Takemori: Dept. of Pharmacology, 3-260 Millard Hall, 435 Delaware St., S.E., University of Minnesota, Minneapolis, MI 55455 **Pharmacological studies with an alkylating narcotic agonist, chloroxymorphamine, and antagonist, chlornaltrexamine.** Journal of Pharmacology and Experimental Therapeutics. 213(3):539-544, 1980.

The binding of 3H-naltrexone to male Swiss-Webster mouse brain homogenates was irreversibly inhibited by chloroxymorphamine (COA) and chlormaltrexamine (CNA), which are the 6-bis(2-chloroethyl)amino derivatives of oxymorphone and naltrexone respectively. Intracerebroventricular (i.c.v.) administration of COA (4nmol) elicited analgesia that lasted four times longer than analgesia produced by an equimolar and equieffective dose of oxymorphone. Analgesia induced by COA could be reversed and blocked by naloxone. COA and CNA (i.c.v.) both antagonized morphine-induced analgesia for 3 days. Total specific binding of 3H-naltrexone was also significantly decreased for 3 days after treatment with CNA or COA. Results suggest that CNA and COA alkylate the opioid receptors to produce antagonist and agonist/antagonist effects, respectively. Results are discussed in relation to mechanisms of tolerance and dependence. 23 references. (Author abstract modified)

004083 Castellani, S.; Adams, P. M. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX 77550 **Effects of dopaminergic drugs on phencyclidine-induced behavior in the rat.** Neuropharmacology. 20(4):371-374, 1981.

The effects of dopaminergic drugs on behavior induced by 2.0, 4.0, or 6.0mg/kg phencyclidine in male Fischer-344 rats were studied. Haloperidol (0.5mg/kg) inhibited phencyclidine-induced stereotypy and locomotor activity, but increased phencyclidine-induced ataxia. Apomorphine (0.2mg/kg) inhibited locomotor activity induced by 2.0mg/kg phencyclidine, but enhanced locomotor activity induced by the larger doses. Apomorphine also potentiated phencyclidine-induced stereotypy. Results indicate that dopaminergic mechanisms are involved in phencyclidine-induced behavior. 23 references. (Author abstract modified)

004084 Chau, Thuy T.; Harris, Louis S. Dept. of Pharmacology, Medical College of Virginia, MCV Station, Box 613, Richmond, VA 23298 **Comparative studies of the pharmacological effects of the d- and l-isomers of codeine.** Journal of Pharmacology and Experimental Therapeutics. 215(3):668-672, 1980.

Comparative studies of the pharmacological effects of the d-isomer and l-isomers of codeine are described. l-Codeine was active in the mouse tail flick test as well as in the hotplate test whether given p.o. or s.c. The d-isomer of codeine was inactive in both tests up to 100mg/kg, but caused hyperexcitability, convulsions, and ultimately death. Although l-codeine was more potent than d-codeine in inhibiting the cough reflex in the anesthetized cat, the d-isomer did have good activity. In these animals, l-codeine did not significantly affect the cardiovascular parameters at the doses tested, whereas d-codeine caused a significant but transient decrease in the blood pressure and heartrate. The specific and nonspecific properties of d-codeine and l-codeine were further delineated in the opiate receptor binding assay. l-Codeine inhibited the stereospecific binding of (3H)dihydromorphine in mouse brain homogenates at loser dosage than did d-codeine. 20 references. (Author abstract modified)

004085 Chen, F. F.; Lin, M. T. Lin: Dept. of Physiology and Biophysics, N.D.M.C., P.O. Box 8244, Taipei, Taiwan 107 **Effects of dopamine, apomorphine, gamma-hydroxybutyric acid, haloperidol and pimozide on reflex bradycardia in rats.** Journal of Pharmacology and Experimental Therapeutics. 214(2):427-432, 1980.

The cardiovascular responses to i.v. doses of epinephrine were assessed in vehicle controlled, dopamine treated, apomorphine treated, GABA treated, haloperidol treated, and pimozide treated rats under urethan anesthesia. Previous exposure to several injections of epinephrine did not change the basal values of arterial pressure and heartrate. Dopaminergic transmission alterations in the brain influenced the reflex bradycardia in response to elevation in arterial pressure. Blockade of brain dopaminergic receptors with either haloperidol or pimozide significantly reduced reflex bradycardia. Either direct activation of central dopaminergic receptors with dopamine and apomorphine or indirect activation with GABA enhanced epinephrine-induced bradycardia. Results indicate that central dopamine systems play a role in the elaboration or modulation of reflex bradycardia. Specifically, brain dopamine appears to facilitate reflex bradycardia, since activation of dopamine systems facilitates and blockade inhibits reflex bradycardia. 27 references. (Author abstract modified)

004086 Clark, M. S. G.; Johnson, A. M.; McClelland, G. R.; Nelson, D. R. Beecham Pharmaceuticals Research Division, Harlow, Essex, England **Pharmacological and biochemical properties of BRL 14342, a novel potential antidepressant drug.** Neuropharmacology. 19(12):1207-1208, 1980.

Pharmacological and biochemical properties of BRL 14342, a novel potential antidepressant drug, are described. The results of animal studies indicate that BRL 14342 is a noradrenaline (NA) and 5-hydroxytryptamine (5-HT) uptake blocker with a low propensity to cause side-effect in vivo. Results also indicate that it should possess significant antidepressant activity with low sedative, anticholinergic, and cardiovascular side-effects. This, together with increased relative potency in tests predictive of therapeutic activity, indicates that BRL 14342 should have a larger margin of tolerance than imipramine. 9 references.

004087 Collier, Harry O. J.; Cuthbert, Nigel J.; Francis, David L. Research Dept., Miles Laboratories Limited, Stoke Poges, Slough, Berkshire, SL2 4LY, England **Character and meaning of quasi-morphine withdrawal phenomena elicited by methylxanthines.** Federation Proceedings. 40(5):1513-1518, 1981.

The character and meaning of quasimorphine withdrawal phenomena elicited by methylxanthines are described. 3-isobutyl-1-methylxanthine (IBMX), theophylline, caffeine, ICI 63197, and RO 201724 are cited as drugs that fulfill the criteria of quasimorphine withdrawal syndrome. It is concluded that these drugs act by inhibiting brain cyclic AMP phosphodiesterase, thus raising the level of cyclic AMP in appropriate neurons. These findings are consistent with the view that the molecular mechanism of opiate dependence is the hypertrophy of a neuronal cyclic AMP system in compensation for the inhibition by opiate of an adenylate cyclase. These studies suggest that: 1) very rapid tests for opiate activity and for addictive liability can be devised by use of IBMX; 2) opiates may be used clinically to counter poisoning by caffeine or theophylline; and 3) a relationship may exist between caffeine consumption and opiate addiction. 22 references. (Author abstract modified)

004088 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Factors regulating drug cue sensitivity: limits of discriminability and the role of a progressively decreasing training dose in fentanyl-saline discrimination.** Journal of Pharmacology and Experimental Therapeutics. 212(3):474-480, 1980.

The roles of physiological sensitivity and of training dose in the apparent sensitivity of rats to the discriminative stimulus properties of the narcotic analgesic fentanyl were examined. Rats were trained to discriminate 0.04 mg/kg of fentanyl from saline in a two lever operant procedure and then were retrained on progressively lower doses of the training drug. Stimulus generalization experiments revealed: 1) that the slope of fentanyl's stimulus generalization gradient is relatively steep at training dose 0.04mg/kg and 0.02mg/kg, but may flatten as the training dose is lowered further; 2) that fentanyl's ED50 value for stimulus generalization is directly proportional to training dose; and 3) that the ED50 is an almost constant fraction of training dose at fentanyl training doses ranging from 0.04mg/ to 0.005mg/kg. It is concluded that training dose is a major determinant of the apparent sensitivity of rats to the discriminative stimulus properties of drugs. 24 references. (Author abstract modified)

004089 Commissaris, R. L.; Semeyn, D. R.; Moore, K. E.; Rech, R. H. Dept. of Psychiatry, Yale University School of Medicine, 34 Park St., New Haven, CT 06508 **The effects of 2,5-dimethoxy-4-methylamphetamine (DOM) on operant behavior: interactions with other neuroactive agents.** Communications in Psychopharmacology. 4(5):393-404, 1980.

The effects of 2,5-dimethoxy-4-methylamphetamine (DOM) and other stimulant and hallucinogenic agents on food reinforced, fixed-ratio operant responding were investigated. It is noted that hallucinogens produce a disruption of this operant responding characterized by long periods of nonresponding (pausing). On the other hand, central stimulant or depressant drugs produce slowed and erratic response rates not characterized by pausing. Coadministration of the hallucinogens d-lysergic acid diethylamide (LSD) and mescaline shifted to the left the dose response curve for the pausing produced by DOM. Coadministration of quipazine and m-chlorophenylpiperazine (MCPP) also shifted to the left the DOM dose response curve. Moreover, coadministration of cinanserin dramatically antagonized the pause producing effect of DOM, as evidenced by an approximately fourfold shift to the right in the dose response curve. Coadministration of the indirect dopamine agonist d-amphetamine or the neuroleptics haloperidol and chlorpromazine failed to alter the dose dependent pausing produced by DOM. These data suggest that the pause producing effects of DOM are related to serotonin agonistic actions of this agent and not to interactions with DA neurons in the brain. 19 references. (Author abstract modified)

004090 Cooper, Steven J.; Burnett, Gary; Brown, Kenneth. Dept. of Psychology, University of Birmingham, Birmingham, B15 2TT England **Food preference following acute or chronic**

chlordiazepoxide administration: tolerance to an antineophobic action. Psychopharmacology. 73(1):70-74, 1981.

The two actions of chlordiazepoxide (CDP) on rats in a food preference test (first, a general appetite enhancing effect; and second, an antineophobic effect) were studied. Following acute injection of CDP, the rats changed from eating predominantly familiar food to a novel food. This may signify an antineophobic effect of CDP. However, following 10 days of treatment with CDP, the antineophobic effect was abolished and the choice of familiar food was enhanced. This could be an indication of a more general appetite enhancing effect. Hence, some form of tolerance may develop to CDP's effects over 10 days of treatment which selectively abolishes antineophobic action while leaving the appetite effect further enhanced. There were no indications of tolerance developing to the actions of CDP in animals familiarized with all the test foods before the preference test was run. Hence the presence of food novelty may be critical to the observation of some form of selective tolerance. 27 references. (Author abstract modified)

004091 Corner, M. A.; Mirmiran, M.; Bour. H. L. M. G.; Boer, G. J.; van de Poll, N. E.; van Oyen, H. G.; Uylings, H. B. M. Netherlands Institute for Brain Research, Amsterdam, The Netherlands **Does rapid-eye-movement sleep play a role in brain development?** Progress in Brain Research. 53:347-356, 1980.

The importance of REM sleep for normal brain development was studied in rats. Daily injections of chlorimipramine were used to suppress REM sleep in rat pups during postnatal weeks 2 and 3. No REM rebound was observed the week after the drug was discontinued. In adulthood, however, treated male rats showed a sizeable increase and intensification of REM sleep. Sexual performance was severely deficient, and open-field performance revealed an abnormally high level of anxiety. Postmortem brain examination revealed a selective enlargement of the hypothalamus in the treated males, along with reduced cell number in the cerebral cortex. In treated females, the hippocampus and cerebral cortex were clearly enlarged and accounted for a significantly higher total brain weight in the experimental group. It is suggested that disturbances in monoamine metabolism can drastically reduce REM sleep during infancy and lead to specific brain and behavior abnormalities in later life. 23 references.

004092 Costall, Brenda; Naylor, Robert J.; Nohria, Virinder. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, BD7 1DP, England **Use of the intracerebral injection technique to elucidate mechanisms of apomorphine climbing and its antagonism in the mouse.** Psychopharmacology. 73(1):91-94, 1981.

Mechanisms of apomorphine climbing and its antagonisms were studied in the mouse using the intracerebral injection technique. Climbing behavior induced by peripherally administered apomorphine in the mouse was reduced by bilateral intraaccumbens fluphenazine, (and -) and (-) sulpiride, and by serotonin, but not by () sulpiride, dl-propranolol, phentolamine, atropine, or methysergide. A specific antagonism of climbing could not be shown when fluphenazine was injected into the striatum, hypothalamus, thalamus, reticular formation, frontal cortex, or cerebellum, but was apparent when a large dose of fluphenazine was placed below (but not above) the accumbens nucleus. 6-Hydroxydopamine denervation of the nucleus accumbens did not alter the climbing antagonism afforded by fluphenazine, although sulpiride was threefold more effective following denervation. The data indicate an accumbens involvement in the climbing phenomenon, that sulpiride more effectively antagonizes climbing after accumbens denervation, and that the presumed dopamine agonist/antagonist interaction in the accumbens, which controls climbing, may also involve serotonergic function. the studies emphasize the value of the intracerebral injection technique to an analysis of drug action in the mouse. 13 references. (Author abstract modified)

004093 Cowan, Alan. Dept. of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **RX 336-M, a new chemical tool in the analysis of the quasi-morphine withdrawal syndrome.** Federation Proceedings. 40(5):1497-1501, 1981.

The pharmacological baselines that link disparate agents that induce wet dog shaking (RX 336-M, AG-3-5, Sgd 8473, thyrotropin releasing hormone (TRH), and sodium valproate) were studied using RX 336-M as the reference shake inducing compound. Peripheral administration of clonidine, haloperidol, d-lysergic acid diethylamide, or morphine suppressed chemically-induced shaking; naloxone had no marked effect. Cross-tolerance interactions were asymmetrical. In view of the unidirectional nature of the cross-tolerance relationships studied, it is concluded that AG-3-5, Sgd 8473, sodium valproate, and TRH initiate wet dog shaking through neural substrates that differ from the one(s) associated with RX 336-M. Nevertheless, all five compounds may eventually trigger a common shake inducing mechanism. 50 references. (Author abstract modified)

004094 Crabbe, J. C.; Young, E. R.; Janowsky, J.; Rigter, H. Medical Research Service, Veterans Administration Medical Center, Portland, OR 97201 **Pyrazole exacerbates handling-induced convulsions in mice.** Neuropharmacology. 20(6):605-609, 1981.

The severity of handling induced convulsions declined in male Swiss-Webster mice over 4 days of testing. Daily injections of pyrazole, an inhibitor of alcohol dehydrogenase, prevented the reduction in convulsions in handled mice. Pyrazole also exacerbated convulsions in mice at initial test sessions. The effects of pyrazole were dose related. 31 references. (Author abstract modified)

004095 Daniel, Stephen A.; Thompson, Travis. Institute of Environmental Medicine, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Methadone-induced attenuation of the effects of delta9-tetrahydrocannabinol on temporal discrimination in pigeons.** Journal of Pharmacology and Experimental Therapeutics. 213(2):247-253, 1980.

Methadone-induced attentuation of the effects of delta9-tetrahydrocannabinol (delta9-THC) on temporal discrimination in pigeons was investigated. Pigeons responded under a discrete trial procedure in which they were required to peck one or two keys depending on the duration of conditional stimulus. Correct choices resulted in the intermittent presentation of food; incorrect choices resulted in a darkened chamber. Intermediate durations were also presented occasionally. Delta9-THC resulted in a dose dependent decrease in accuracy with the greater effect on long duration trials. Repeated methadone alone resulted in a decrease in accuracy only when the methadone dose was changed. High doses of methadone resulted in either a complete or partial attenuation of effects of THC on temporal discrimination accuracy as compared to a low methadone dose or THC alone. Results suggest the possibility of cross-tolerance or antagonism between methadone and THC. 45 references. (Author abstract modified)

004096 Das, M.; Ganguly, D. K.; Vedasiromoni, J. R. Div. of Pharmacology and Experimental Therapeutics, Indian Inst. of Experimental Med., 4, Raja S. C. Mullick Road, Calcutta-700 032, India **Anti-tremor action of C10Dichol, a peripheral acetylcholine synthesis inhibitor.** British Journal of Pharmacology. 71(1):349-353, 1980.

The antitremor action of decamethylene bis-(hydroxyethyl)-dimethylammonium bromide (C10Dichol), a peripheral acetylcholine synthesis inhibitor, was investigated. C10Dichol inhibited tremor induced by oxotremorine, nicotine, and physostigmine and afforded partial protection from physostigmine-induced mortality in mice. In nonparalyzing doses, C10Dichol antagonized the neuromuscular effects of oxotremorine, nicotine, and physostigmine. Pretreatment with C10Dichol did not prevent tremor and neuromuscular paralysis induced by harmine or arecoline. These findings indicate it may be possible to develop peripherally acting drugs for the treatment of Parkinson's disease. 26 references. (Author abstract modified)

004097 Davis, Hasker P.; Rosenzweig, Mark R.; Kinkade, Patrick T.; Bennett, Edward L. New York Hospital, Cornell Medical Center, Dept. of Neurology, 525 East 68th St., New York, NY 10021 **Effects of anisomycin on retention of the passive-avoidance habit as a function of age.** Experimental Aging Research. 7(1):33-44, 1981.

Three age groups of male Swiss albino CD-1 mice (2 to 3 months, 6 to 7 months, and 14 to 15 months) were treated with a 120mg/kg dose of the protein synthesis inhibitor anisomycin or with an equal volume of saline at various times before and after training (20 min pretraining and 0, 10, 30, or 180 min posttraining) in a shock motivated passive-avoidance task. Young and intermediate aged mice treated before or after training demonstrated impaired retention at a 7 day test, but retention was normal for Ss injected 10, 30, or 180 min posttraining. The older mice showed similar results with one exception: there is a reduction in the incorporation of (1-14C) leucine into the synaptosomal brain fraction of 12-month-old mice as compared to the 3-month-old mice. The prolonged gradient of retrograde amnesia demonstrated in older Ss could not be accounted for by impaired acquisition, impaired short-term memory, altered spontaneous locomotor activity, or differential inhibition of brain protein synthesis. 24 references. (Author abstract modified)

004098 Davis, John D.; Wirtshafter, David; Asin, Karen E.; Brief, Deborah. Psychology Dept., University of Illinois, Chicago, IL 60680 **Sustained intracerebroventricular infusion of brain fuels reduces body weight and food intake in rats.** Science. 212(4490):81-83, 1981.

The effects of long-term intracerebroventricular infusions of glucose, glycerol, and beta-hydroxybutyrate on both food intake and bodyweight of the rat were studied. A stabilization of bodyweight at a lower than normal level occurred. Among the glucose treated and glucerol treated animals this weight loss was caused in part by temporary hypophagia. Among the animals treated with beta-hydroxybutyrate the weight loss was unaccompanied by a reduction in food intake. The results are consistent with the view that the systems controlling food intake and bodyweight are sensitive to the availability of brain fuels. They are not consistent, however, with the view that these control systems monitor calories independently of their source. 21 references. (Author abstract modified)

004099 Davis, Kenneth L.; Rosenberg, Gordon S. Bronx V.A. Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468 **Induction of behavioral supersensitivity to apomorphine by DFP treatment.** Life Sciences. 28(17)1953-1959, 1981.

The effect of diisoflurophosphate (DFP), a long-acting inhibitor of acetylcholinesterase, on apomorphine-induced climbing behavior, was tested in mice. Twelve hours following intraperitoneal administration of a single dose of DFP, animals demonstrated a significant increase in apomorphine-induced climbing behavior. This effect was not observed 24 hours following DFP pretreatment. Results suggest that acute administration of a cholinomimetic agent, may produce behavioral supersensitivity to dopamine agonists. 42 references. (Author abstract modified)

004100 Dawbarn, D.; Harmar, A. J.; Pycock, C. J. Dept. of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **Intranigral injection of capsaicin enhances motor activity and depletes nigral 5-hydroxytryptamine but not substance P.** Neuropharmacology. 20(4):341-346, 1981.

Locomotor activity in female Porton rats was enhanced for up to 6 days after bilateral injections in the pars reticulata of the substantia nigra of 30mcg capsaicin dissolved in dimethyl sulphoxide (DMSO), compared to the activity of DMSO sham injected controls. Capsaicin also reduced the cataleptic effects of fluphenazine. Nigral concentrations of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid were decreased and striatal and nucleus accumbens levels of dopamine metabolites were increased on days 1 and 3 after intranigral capsaicin injection. No changes in nigral substance-P content were observed after intranigral injection of capsaicin. 26 references. (Author abstract modified)

004101 De Lima, Thereza C. M.; Palermo-Neto, Joao. Laboratorio de Farmacologia, Universidade Federal de Santa Catarina, Rua: Ferreira Lima, 26 - Florianopolis, S.C. - CEP 88,000, Brazil **Effects of withdrawal from long-term diphenylhydantoin treatment on audiogenic and maximal electroshock-induced seizures in rats.** Acta Neurologica Scandinavica. 63(3):189-196, 1981.

The effects of diphenylhydantoin (DPH) withdrawal on rats' reactions to maximal electroshock and sound were investigated. Animals were more sensitive to convulsions elicited by maximal electroshock at 48 hours after drug removal and more sensitive to convulsions elicited by sound 72 hours after drug removal. Results of experiments with food deprived rats show that the cause of this sensitivity is not vitamin B6 deficiency. Results suggest that long-term DPH treatment might develop a central nervous system supersensitivity state. 29 references. (Author abstract modified)

004102 Dhumal, V. R.; Bhavsar, V. H. Pharmacology Dept., Government Medical College, Surat - 395 001, India **Antagonism of some central effects of d-tubocurarine by gamma-aminobutyric acid.** Archives Internationales de Pharmacodynamie et de Therapie. 248(1):148-153, 1980.

Intracerebroventricular (i.c.v.) administration of d-tubocurarine (dtc) to rats produced seizures which could be blocked by i.c.v. administration of GABA or i.p. administration of hydroxylamine. GABA was not effective after i.p. administration. Local application of dtc to the spinal cord of decerebrate dogs facilitated the scratch reflex, whereas GABA application inhibited the scratch reflex. It is concluded that the excitatory effects of dtc on the CNS may be due to inhibition of a naturally occurring inhibitory substance such as GABA or a closely related compound. 6 references. (Author abstract modified)

004103 Donovick, Peter J.; Burright, Richard G.; Fanelli, Richard J.; Symchowicz, Beatrice; Ritz, Andrew. Dept. of Psychology, SUNY, Binghamton, NY 13901 **Cocaine and seizure protection in mice of varying brain weights.** Pharmacology Biochemistry and Behavior. 14(3):409-414, 1981.

The effects of cocaine on seizures were studied in mice genetically selected for different brain weights. Fuller low brain weight mice were more susceptible to seizures induced by transcorneal shock and exhibited more severe seizures than Fuller medium and high brain weight mice or mice of Binghamton Heterogeneous stock. Cocaine hydrochloride (5, 10, or 20mg/kg) provided protection against seizures in a dose dependent fashion, particularly in medium brain weight and Heterogeneous stock mice. Repeated daily doses of cocaine (10mg/kg) also decreased the severity of seizures induced by transcorneal shock. 23 references. (Author abstract modified)

004104 Dum, Jane; Blasig, Julia; Herz, Albert. Herz: Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000, Munchen 40, West Germany **Buprenorphine: demonstration of physical dependence liability.** European Journal of Pharmacology. 70(3):293-300, 1981.

Male Sprague-Dawley rats treated chronically with buprenorphine (0.5mg/kg twice daily for 4 days) developed complete tolerance to the antinociceptive effects of the drug, but showed only weak signs of withdrawal upon cessation of buprenorphine treatment or naloxone challenge. More intense withdrawal signs were observed when buprenorphine treatment was followed by substitution treatment with morphine. A single 10mg/kg injection of morphine 12 hours after the last buprenorphine injection enabled naloxone precipitation of withdrawal, even though naloxone did not precipitate withdrawal after this dose of morphine in naive rats. Results indicate that buprenorphine does induce limited dependence. The weakness of the withdrawal signs produced by buprenorphine in direct dependence tests is probably due to the slow dissociation of the drug from the receptor. 14 references. (Author abstract modified)

004105 Dumont, C.; Laurent, J.; Grandadam, A.; Boissier, J. R. Centre de Recherches Roussel-Uclaf, F-93230 Romainville, France **Anorectic properties of a new long acting serotonin uptake inhibitor.** Life Sciences. 28(17):1939-1945, 1981.

RU 25591 (6,7,8,9-tetrahydro N,N-dimethyl 5-(4-nitrophenyl) oxy 5H-benzocyclohepten 7-amine) cis, fumarate, a potent, selective and long-acting serotonin uptake inhibitor was examined for anorectic properties. It was found that RU 25591 reduced food intake in rats, dogs, and pigs. Kinetics in single dosed animals showed that the duration of RU 25591 food intake depression was shorter than in vivo serotonin uptake inhibition. In repeated dosing treatment, a progressive time related decrease in the inhibition of food consumption was observed which was more evident in pigs than in dogs. The anorectic activity of RU 25591 does not depend exclusively on its ability to block serotonin uptake. However, available biochemical results do not permit exact specification of its mechanism of action. 27 references. (Author abstract modified)

004106 Dykstra, Linda A. Dept. of Psychology 013A, University of North Carolina, Chapel Hill, NC 27514 **Discrimination of electric shock: effects of some opioid and nonopioid drugs.** Journal of Pharmcology and Experimental Therapeutics. 213(2):234-240, 1980.

The effects of some opioid analgesics (methadone, propoxyphene, pentazocine, cyclazocine and nalorphine) were examined on the discrimination of electric shock in squirrel monkeys. Discrimination of the presence of absence of shock was studied at two different shock intensities: 1) an intensity below which squirrel monkeys maintain a shock under schedules of shock titration; and 2) an intensity determined to be close to each monkey's discrimination threshold. Methadone, pentazocine, cyclazocine, and nalorphine but not propoxyphene decreased to the percentage of correct response at both shock intensities, without altering percentage of correct responses in the absence of shock. It appears that drug-induced alterations in the percentage of correct responses in the presence of shock are related to the physical properties of the shock, with lower intensities affected more than higher intensities. 36 references. (Author abstract modified)

004107 Dzhaliashvili, T. A.; Akhalkatsi, R. G.; Iordanishvili, G. S.; Ayvazashvili, I. M. Institut fiziologii im. I. S. Beritashvili, Akademiya nauk GruzSSR, Tbilisi, USSR **/A study of the effect of neuropharmacological drugs on the functional activity of rat brain./** Issledovaniye vliyaniya neyrofarmakologicheskikh veshchestv na funktsional'nuyu aktivnost' golovnogo mozga krys. Ukrainskiy Biokhimicheskiy Zhurnal. 53(2):109-114, 1981.

The effect of neuropharmacological drugs on the functional activity of the rat brain was studied in relation to RNA synthesis and animal behavior. Phosphodiesterase, adenyl cyclase, and monoaminoxidase activity in glial cells was investigated. Results show that glial cells have high phosphodiesterase, adenyl cyclase and monoaminoxidase-A activity. The neuropharmacological drugs, reserpine and transamine, affect RNA synthesis in vivo, but have no effect in vitro. Transamine and reserpine accelerate the formation of the conditioned defensive reflex, but they strongly inhibit the reproduction of this reflex. 21 references. (Journal abstract)

004108 Elmazar, M. M. A.; Sullivan, F. M. Sullivan: Dept. of Pharmacology, Guy's Hospital Medical School, London SE1 9RT, England **Effect of prenatal phenytoin administration on brain tryptophan metabolism of rat offspring during the preweaning period.** Journal of Pharmacy and Pharmacology. 32(10):697-700, 1980.

Brain tryptophan metabolism was studied in offspring of Wistar rats treated with phenytoin (100mg/kg/day) on days 7 to 19 of pregnancy. Serum tryptophan and brain concentrations of tryptophan, 5-hydroxytryptamine, and 5-hydroxyindoleacetic acid were above control levels at 3 days of age, but not at 4, 15, or 21 days of age. The effect of prenatal phenytoin exposure was not apparent at 3 days of age in pups cross-fostered to control mothers at 2 days of age. Results suggest that the altered brain tryptophan metabolism observed in offspring of phenytoin treated rats was mediated through changes in lactation or nursing ability of the mothers. 21 references. (Author abstract modified)

004109 Endroczi, E. Central Research Division, Postgraduate Medical School, Budapest, Hungary **ACTH-like peptides, pituitary-adrenocortical function and avoidance behavior.** Progress in Brain Research. 53:111-121, 1980.

The interactions of ACTH-like peptides (ALP), cholinomimetics, and opiates on corticotropin releasing hormone (CRH) secretory elements are reviewed. The role of noradrenergic and opiate receptor mechanisms in the behavioral effects of ALP are also discussed. Effects of dibutyryl cyclic GMP on CRH release and on behavior are described. Studies of pituitary/adrenocortical function indicate that cholinergic and opiate mechanisms are involved in activation of CRH neurosecretory elements. Data from studies of extinction of avoidance responses in rats indicate that ALP exert multiple action on cells with different receptive sites and that activation of brain noradrenergic systems is not necessarily coupled to extinction of conditioned responses. 34 references.

004110 Engel, Jorgen; Berggren, Ulf. no address **Effects of lithium on behaviour and central monoamines.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):133-143, 1980.

Biochemical and behavioral studies of the effects of acute lithium administration on central catecholamine mechanisms are described. Acute administration of lithium: 1) specifically suppressed a conditioned avoidance behavior in rats; 2) markedly reduced amphetamine-induced locomotor stimulation in mice; and 3) caused a significant reduction of catecholamine synthesis but not serotonin synthesis in rats. The finding that the administration of L-DOPA counteracts the behavioral effects of lithium indicates a causal relationship between the behavioral and biochemical effects of acute lithium administration and supports the contention that lithium may act by interfering with central catecholaminergic mechanisms. Taken together with previous findings, these data cast doubt upon the contention that lithium acts by directly inhibiting tyrosine hydroxylase. A panel discussion of these findings is appended. 21 references.

004111 Ervin, Gregory N.; Birkemo, Larry S.; Nemeroff, Charles B.; Prange, Arthur J., Jr. Biological Sciences Research Center, Dept. of Psychiatry, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **Neurotensin blocks certain amphetamine-induced behaviours.** Nature. 291(5810):73-76, 1981.

The behavioral effects of bilateral injections of either neurotensin (NT) or haloperidol (HA) into the nucleus accumbens of rats were investigated. Such injections markedly diminished the forward locomotion and rearing induced by a d-amphetamine (AM). Neither NT nor HA affected the insomnia or sniffing component of AM arousal. Isovolumetric intraaccumbens injections of artificial CSF or the endogenous decapeptide, luteinizing hormone releasing hormone (LHRH) did not affect AM behaviors. It is suggested that the observed effects of NT and HA in AM treated rats probably were not due to impaired motor function per se, since intraaccumbens injections of NT or HA neither altered forward locomotion or rearing in untreated rats placed in an open field nor a variety of reflex activities. In contrast, NT did not produce neuroleptic-like effects when injected into nucleus caudatus; HA blocked stereotyped sniffing, licking, biting, and head bobbing observed after AM, but NT did not. Since NT and dopamine are present in substantial quantities in the nucleus accumbens, it is suggested that NT may act in the nucleus accumbens to modulate dopaminergic function. 21 references. (Author abstract modified)

004112 Fink, J. Stephen; Reis, Donald J. Reis: Lab. of Neurobiology, Dept. of Neurology, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Genetic variations in midbrain dopamine cell number: parallel with differences in responses to dopaminergic agonists and in naturalistic behaviors mediated by central dopaminergic systems. (Unpublished paper).** Research Report, NIMH Grant 5RO1-MH-33190, 1980. 36 p.

Mice of the BALB/cJ and CBA/J strains were compared with respect to the magnitude of the behavioral responses to two dopamine (DA) agonists with differing modes of action: amphetamine, a drug whose action is largely mediated by releasing DA presynaptically; and apomorphine, a drug whose behavioral actions are principally mediated by direct activation of DA receptors. The mice strains were examined for differences in spontaneous locomotion and exploration, both behaviors being dependent on DA systems. Since the locomotor effects of amphetamine and exploration are largely mediated by mesolimbic (A10) neurons, the activity of tyrosine hydroxylase (TH) was compared between strains in regions receiving that innervation. A variety of differences were noted between the strains, and the findings indicate genetic variations in the neurochemical parameters of neurotransmitter content, turnover, and biosynthetic enzyme activity correlated with behavior and drug response. The results raise the possibility that variations in numbers of neurons of a particular chemical class may be the common biological denominator which underlies genetically determined differences in the content of their neurotransmitters and/or their synthesizing enzymes. The findings may also have clinical relevance with respect to degenerative disorders of the CNS, such as Parkinson's disease. 39 references.

004113 Forster, Christine; Parkes, Janet; Cox, B. Dept. of Pharmacology, Materia Medica and Therapeutics, Manchester University Medical School, Manchester M13 9PT, England **Effects of olfactory bulbectomy and peripherally-induced anosmia on thermoregulation in the rat: susceptibility to antidepressant type drugs.** Journal of Pharmacy and Pharmacology. 32(9):630-634, 1980.

The mechanism underlying the thermoregulatory deficit in male Sprague-Dawley rats observed at low ambient temperatures after olfactory bulbectomy was studied. Rats made peripherally anosmic with zinc sulfate did not show a thermoregulatory deficit, which suggests the deficit observed after surgical ablation of the olfactory bulbs is not related to anosmia per se. The abnormal response to cold in bulbectomized animals was blocked by chronic daily administration of amitriptyline (10mg/kg), mianserin (10mg/kg), or the 5-hydroxytryptamine (5-HT) uptake inhibitor Org-6582 (10mg/kg) for 7 days. It is suggested that serotonergic mechanisms may be involved in the thermoregulatory deficit and other behavioral changes observed after olfactory bulbectomy. 16 references. (Author abstract modified)

004114 Foster, John A.; Morrison, M.; Dean, S. J.; Hill, M.; Frenk, H. 23272 Strathern St., Canoga Park, CA 91304 **Naloxone suppresses food/water consumption in the deprived cat.** Pharmacology Biochemistry and Behavior. 14(3):419-421, 1981.

The opiate antagonist naloxone hydrochloride decreased food and water consumption in six drug naive cats. Food consumption during a 1 hour period after 23 hours of deprivation decreased significantly in all six cats in linear relationship to increasing dose (1mg/kg and 10mg/kg i.p.) of naloxone. Water consumption decreased below control in a linear relationship to increasing dose of naloxone for five of the six cats. These results, as well as behavioral signs (vomiting, vocalization, salivation, mydriasis, moderate catatonia, and hissing) occasionally exhibited by four of the cats, suggest that naloxone may induce malaise. 23 references. (Author abstract modified)

004115 Fregnan, G. B.; Chieli, T. Divisione Ricerche Lusofarmaco, Via Carnia 26, I-20132 Milano, Italy **Classical neuroleptics and deconditioning activity after single or repeated treatments: role of different cerebral neurotransmitters.** Arzneimittel-Forschung. 30(11):1865-1870, 1980.

A dose dependent inhibition of conditioned avoidance response (CAR) was documented in trained rats after acute treatment with several neuroleptics: haloperidol; chlorpromazine (CPZ); fluanisone; and 4-p-fluorophenyl-5-N(N'-o-methoxyphenyl)piperazinoethyl-4-oxazolin-2-one(zoloperone, LR 511). The compounds differently affected the unconditioned escape response (UER); haloperidol and LR 511 were least active. Daily treatment with LR 511 or haloperidol for 7 to 16 days did not cause tolerance, and increased the effects of these drugs on CAR and on UER. This supersensitivity did not disappear after more than 30 days without neuroleptic treatment. The effects of acute neuroleptic administration in combination with other centrally active drugs are noted. The role of various neurotransmitters is discussed. 30 references. (Author abstract modified)

004116 Fregnan, G. B.; Porta, R. Divisione Ricerche, Lusofarmaco S.p.A., Via Carnia 26, I-20132 Milano, Italy **A comparison between some biochemical and behavioural effects produced by neuroleptics.** Arzneimittel-Forschung. 31(1):70-74, 1981.

The effect is discussed of a new neuroleptic drug, 4-p-fluorophenyl-5-N(N'-o-methoxy-phenyl)piperazinoethyl-4-oxazolin-2-one (LR 511), on homovanillic acid (HVA) levels of the corpus striatum (CS) and tuberculum olfactorium (TO) of rat brain.

Dopamine (DA) and noradrenaline (NA) levels were determined, and comparative evaluations were made between the conditioned avoidance response test and the catalepsy test. Acute administration of five neuroleptic drugs to rats produced a dose dependent increase in brain HVA which was of greater magnitude and of longer duration in the CS than in the TO. LR 511 appeared to be 5 to 10 times more potent than were fluanisone and clozapine, was as active as was chlorpromazine (CPZ), and was about twenty times less active than was haloperidol. Time course studies on DA turnover indicated that LR 511 at a moderate dosage has some similarities with clozapine (such as a lower difference between striatal and limbic tissues). All the neuroleptics inhibited the conditioned avoidance response and at their ED50s (confidential limits) on this parameter (excluding clozapine) caused an equal increment of the cerebral HVA level. At their ED50s on catalepsy, the neuroleptic drugs evoked HVA changes which varied according to the drug tested. Potent cataleptogenic agents either caused strong stimulation of the DA turnover in both brain structures (haloperidol and CPZ) or caused weak stimulation only in the CS (fluanisone). A poor cataleptogenic agent, such as LR 511, was accompanied by the highest HVA levels, and the noncataleptogenic clozapine at the dose of 40mg/kg increased the cerebral HVA levels. It is suggested that the blockade of DA receptors in brain of rodents by a novel drug cannot be considered as a positive prediction of therapeutic efficacy and of clinical potency even when classical neuroleptics are examined. 40 references. (Journal abstract modified)

004117 Fung, Yiu K.; Uretsky, Norman J. Uretsky: Div. of Pharmacology, Ohio State University, College of Pharmacy, Lloyd Parks Hall, 500 W. 12th Ave., Columbia, OH 43210 **The effect of dopamine uptake blocking agents on the amphetamine-induced circling behavior in mice with unilateral nigro-striatal lesions.** Journal of Pharmacology and Experimental Therapeutics. 214(3):651-656, 1980.

The effects of the dopamine (DA) uptake blocking agents, benztropine, cocaine, nomifensine, and mazindol, were studied on the amphetamine-induced circling behavior in mice that received a unilateral nigrostriatal lesion with 6-hydroxydopamine. When administered intrastriatally to these animals, none of the DA uptake inhibitors elicited net circling. However, they inhibited circling induced by amphetamine. In contrast, these agents had no effect on the circling produced by apomorphine in mice that received an electrolytic lesion destroying one striatum. In biochemical studies in vitro, all the DA uptake blocking agents inhibited the stimulatory effects of amphetamine on (3H)DA synthesis and release in mouse striatal slices. It is concluded that if the amount of (3H)DA released into the medium in vitro reflects the amount of DA released from nerve terminals in the striatum in vivo then the inhibitory effect of the uptake blocking agents and EGTA on (3H)DA synthesis and/or release induced by amphetamine could account for their inhibitory effects on amphetamine-induced circling. 36 references. (Author abstract modified)

004118 Gebhart, G. F.; Lorens, Stanley A. Dept. of Pharmacology, University of Iowa, Iowa City, IA 52242 **Attenuation of pethidine-induced antinociception by zimelidine, an inhibitor of 5-hydroxytryptamine reuptake.** British Journal of Pharmacology. 70(3):411-414, 1980.

Morphine and pethidine-induced antinociception was studied in the hot plate and tail flick tests in male Sprague-Dawley rats after selective inhibition of 5-hydroxytryptamine (5-HT) reuptake by fluoxetine or zimelidine. Pretreatment with fluoxetine or zimelidine potentiated the antinociceptive effect of 4.5mg/kg morphine (as base); zimelidine did not alter the effect of 3.0mg/kg morphine. Pethidine-induced antinociception was attenuated or prevented by pretreatment with zimelidine, but not fluoxetine. Results suggest that 5-HT is involved in the expression of morphine-induced analgesia and that morphine and pethidine have different modes of action. 12 references. (Author abstract modified)

004119 Goldberg, Steven R. NIDA, Addiction Research Center, P.O. Box 12390, Lexington, KY 40583 **Histamine as a punisher in squirrel monkeys: effects of pentobarbital, chlordiazepoxide and H1- and H2-receptor antagonists on behavior and cardiovascular responses.** Journal of Pharmacology and Experimental Therapeutics. 214(3):726-736, 1980.

The effects of pentobarbital, chlordiazepoxide, and H1 receptor and H2 receptor antagonists on behavior and cardiovascular responses were investigated in squirrel monkeys. Squirrel monkeys pressed a key under a two component, 30 response fixed-ratio schedule of food presentation. In both nonpunishment and punishment components, every 30th response resulted in food presentation. In the punishment component, the 11th and 22nd response in each 30 response fixed-ratio also produced a 200msec i.v. injection of 30mcg/kg to 100mcg/kg of histamine. This resulted in about an 80% suppression of responding in the punishment component. Behavior suppressed by histamine could be markedly increased by presession treatment with pentobarbital or chlordiazepoxide. Presession treatment with the H1 receptor antagonist, diphenhydramine, reversed the punishment effects of histamine, but enhanced the cardiovascular effects of histamine. In contrast, the H2 receptor antagonist, cimetidine, failed to reverse the punishment effects of histamine, but markedly attenuated the cardiovascular effects of histamine. 34 references. (Author abstract modified)

004120 Goldstein, Menek; Lew, Jow Y.; Engel, Jorgen. Neurochemistry Laboratories, Dept. of Psychiatry, New York University Medical Center, New York, NY 10016 **Relevance of dopamine receptor binding studies for evaluation of antiparkinsonian drugs.** In: Hanin, I., Physico-chemical methodologies in psychiatric research. New York, Raven Press, 1980. 265 p. (p. 103-109).

The potencies of dopamine (DA) agonists in animal models of parkinsonism were compared with their binding affinities to DA receptors. Several antiparkinsonian agents had high binding affinities for DA receptors. In monkeys and rats, the antiparkinsonian potencies of a homologous series of ergoline derivatives correlated with their binding affinities to DA receptor agonist sites. Guanosine triphosphate inhibited the binding of ergolines to DA receptors, and its inhibitory potency was enhanced in the decorticated striatum. Specific binding to DA receptors in decorticate striatum may be a better index of DA agonist potency than binding in the intact striatum. 13 references.

004121 Goudie, Andrew J.; Demellweek, Colin. Psychology Dept., Liverpool University, P.O. Box 147, Liverpool L69 3BX, England **Naloxone fails to block amphetamine-induced anorexia and conditioned taste aversion.** Journal of Pharmacy and Pharmacology. 32(9):653-656, 1980.

Naloxone failed to antagonize anorexia or conditioned taste aversion induced by d-amphetamine in female albino rats. Naloxone also failed to show any direct effects on food intake. Since these findings are not consistent with some previous reports, it is concluded that naloxone antagonism of amphetamine is not a reliable method for studying the interaction of endorphins and catecholamines in the control of behavior. 28 references.

004122 Greenblatt, E. N.; Coupet, J.; Rauh, E.; Szucs-Myers, V. A. CNS Biology Dept., Medical Research Division, American Cyanamid Co., Lederle Laboratories, Pearl River, NY 10965 **Is dopamine antagonism a requisite of neuroleptic activity?** Archives Internationales de Pharmacodynamie et de Therapie. 248(1):105-119, 1980.

Although cis-5,6-dimethoxy-2-methyl-3-(2-(4-phenyl-1-piperazinyl)-ethyl)indolin e(DHO) exhibited a pharmacological profile characteristic of neuroleptic drugs in laboratory animals, it did not alter dopamine (DA) levels, DA turnover rate, or DA stimulated cyclase. DHO induced ptosis and catalepsy, decreased locomotor activity, antagonized amphetamine-induced lethality, and inhibited conditioned avoidance responses. It did not antagonize amphetamine-induced stereotyped behavior or apomorphine-induced gnawing, which are believed to be DA dependent behaviors. The agent decreased the level of norepinephrine in the forebrain. Results suggest that DA antagonism may not be a prerequisite for neuroleptic activity and that the DA hypothesis of schizophrenia may not be valid in all cases. 37 references. (Author abstract modified)

004123 Griffiths, Roland R.; Wurster, Richard M.; Brady, Joseph V. Division of Behavioral Biology, Johns Hopkins University School of Medicine, 720 Rutland Ave., Baltimore, MD 21205 **Choice between food and heroin: effects of morphine, naloxone, and secobarbital.** Journal of the Experimental Analysis of Behavior. 35(3):335-351, 1981.

Baboons responded on a choice task in which discrete trials involved choosing between an intravenous injection of heroin or the availability of food pellets. An intertrial interval of 3 hours followed the completion of each trial. Typically, animals chose heroin on three or four trials a day and chose food on the remaining trials. Animals tended to space the selection of heroin rather than choosing heroin on consecutive trials. A series of single day experimental manipulations was undertaken. Manipulation of the heroin dose produced shifts in the relative frequency of choosing the drug option which were related inversely to dose. Manipulation of number of pellets per food trial produced little change in choice distribution. Noncontingent administration of morphine produced dose related decreases in relative frequency of heroin choice, and at higher doses noncontingent morphine administration decreased the number of trials completed. Noncontingent naloxone administration produced dose related increases in the relative frequency of heroin choices. Noncontingent administration of secobarbital had no effect and high doses reduced the number of trials completed per day. The results suggest that morphine and naloxone produce shifts in this choice behavior by selectively interacting with the reinforcing properties of the option involving heroin. 21 references. (Author abstract modified)

004124 Grilly, David M. Dept. of Psychology, Cleveland State University, Cleveland, OH 44115 **A signal detection analysis of morphine effects on the response bias of rats in a two-shock discrimination task.** Life Sciences. 28(17):1883-1888, 1981.

Signal detection theory techniques were used to assess the extent to which morphine affects response bias of rats in a two choice shock discrimination task. The ratio of low shock (noise) to high shock (signal) trials was varied to produce different response biases prior to drug administration. Morphine significantly reduced signal sensitivity (d') under all three conditions without systematically affecting any of the measures of response bias assessed in this study. While consistent with most reports with respect to d', these results conflict with a few previous reports of morphine disrupting performance more when the discriminative stimulus is the presence of shock than when it is the absence of shock. 12 references. (Author abstract)

004125 Gugushvili, L. N.; Dzhafarli, M. T. no address **/The effect of thioproperazine on delayed reactions in lower monkeys./** Vliyaniye mazheptila na otsrochennyye reaktsii u nizshikh obez'yan. Soobshcheniya Akademii Nauk Gruzinskoy SSR. 99(3):681-684, 1980.

The effect of thioproperazine on short-term image memory in the pig-tailed macaque was studied by the delayed reaction method with restricted movement. Results show that: 0.01mg/kg of thioproperazine improved the ability to solve delayed reaction tasks for about 48 hours; in large doses it reduced this ability for 24 to 72 hours; 0.005mg/kg increased the percentage of correct delayed reactions for about 10 hours. These results support the view that moderate quantities of phenothiazines, adsorbed on the outer surface of the neuronal membranes as a result of conformational changes, can occupy such a position in the membrane pores that they significantly stabilize the presynaptic membrane. 9 references. (Journal abstract modified)

004126 Hallberg, Helene; Almgren, Olle; Engel, Jorgen; Jonason, Jan. Research Laboratories, AB Hassle, S-43183 Molndal, Sweden **Effects of propranolol on the locomotor stimulation induced by activation of postsynaptic catecholamine receptors.** Psychopharmacology. 72(3):227-231, 1981.

The effects of d-propranolol and dl-propranolol on the locomotor stimulation induced by apomorphine and clonidine in reserpinized male NMRI mice were studied in photocell activity chambers. Pretreatment with dl-propranolol prolonged the duration of apomorphine-induced locomotor stimulation without affecting the maximal level of activity. A similar tendency was seen after pretreatment with d-propranolol, which has much lower beta-receptor blocking activity. Clonidine potentiation of apomorphine-induced stimulation in reserpinized mice was reduced dose dependently by pretreatment with dl-propranolol, but not by the administration of d-propranolol. Results suggest that central beta-adrenoceptors are involved in the stimulation induced by apomorphine plus clonidine in reserpinized mice. 17 references. (Author abstract modified)

004127 Harris, R. Adron. Dept. of Pharmacology, University of Missouri School of Medicine, Columbia, MO 65212 **Interactions between narcotic agonists, partial agonists and antagonists evaluated by schedule-controlled behavior.** Journal of Pharmacology and Experimental Therapeutics. 213(3):497-503, 1980.

In male Long-Evans rats responding under a fixed-interval, 5 minute schedule of food presentation, morphine, butorphanol, cyclazocine, ketocyclazocine, ethylketocyclazocine, and N-allylnorphenazocine (SKF-10,047) decreased the average rate of responding in a dose dependent manner. The rate decreasing effects of morphine were markedly antagonized by naltrexone, whereas the effects of SKF-10,047 or high doses of cyclazocine were not antagonized by naltrexone or naloxone. Naltrexone and naloxone caused a moderate antagonism of the effects of butorphanol, ketocyclazocine, ethylketocyclazocine, and low doses of cyclazocine. The classification of these drugs into three groups on the basis of their interaction with the narcotic antagonists is consistent with the proposed existence of three distinct opiate receptor types (mu-receptors, kappa-receptors, and alpha-receptors). 24 references. (Author abstract modified)

004128 Hayashi, Tetsu; Ohashi, Kyoichi; Tadokoro, Sakutaro. Behavior Research Institute, School of Medicine, Gunma University, Maebashi 371, Japan **Conditioned drug effects of d-amphetamine- and morphine-induced motor acceleration in mice: experimental approach for placebo effect.** Japanese Journal of Pharmacology. 30(1):93-100, 1980.

The effects of chronic treatment with 2.5mg/kg d-amphetamine sulfate or 10mg/kg morphine hydrochloride on ambulatory activity were studied in male ddG mice. Half of the animals were exposed to a flickering light (FL) after drug or saline administration. The motor accelerating effects of both drugs were enhanced with repeated administration. In mice treated with either drug 10 times, physiological saline injections elicited the motor acceleration effect for a short time, particularly in mice exposed to FL. This effect disappeared after repeated administration or saline solution for 6 days. The motor accelerating effect induced by saline appeared to be due to the association of conditioned stimuli (the FL and other environmental factors) and drug effects. 14 references. (Author abstract modified)

004129 Heikkila, R. E.; Shapiro, B. S.; Duvoisin, R. C. Dept. of Neurology, College of Medicine and Dentistry of New Jersey, Rutgers Medical School, Piscataway, NJ 08854 **The relationship between loss of dopamine nerve terminals, striatal (3H)spiroperidol binding and rotational behavior in unilaterally 6-hydroxydopamine-lesioned rats.** Brain Research. 211(2):285-292, 1981.

Female Sprague-Dawley rats that showed significant rotational behavior in response to L-DOPA 5 weeks after unilateral 6-hydroxydopamine (6-OHDA) lesions had more specific 3H-spiroperidol binding in the lesioned striatum than in the nonlesioned striatum and had at least 90% destruction of dopamine (DA) terminals in the lesioned striatum. Animals that did not rotate in response to L-DOPA after unilateral 6-OHDA lesions had considerably less destruction of DA terminals and no significant increase in specific binding on the lesioned side. Results are discussed in relation to the response to L-DOPA of patients with Parkinson's disease. 9 references. (Author abstract modified)

004130 Heikkila, Richard E. Dept. of Neurology, College of Medicine and Dentistry of New Jersey, Rutgers Medical School, University Heights, Piscataway, NJ 08854 **Differential effects of several dopamine uptake inhibitors and releasing agents on locomotor activity in normal and in reserpinized mice.** Life Sciences. 28(17):1867-1873, 1981.

Several drugs that were potent dopamine uptake inhibitors in vitro (including GBR 13,069 and GBR 13,098, amfonelic acid, mazindol, Win 35,065 and Win 35,428) were found to cause large increases in locomotor activity in normal mice but not in reserpinized mice. Additionally, these drugs given to reserpinized mice prior to the dopamine releasing agent d-amphetamine, were able to prevent the normal increase in activity caused by d-amphetamine. The data demonstrate markedly different in vivo effects of dopamine uptake inhibitors and dopamine releasing agents. 11 references. (Author abstract)

004131 Helmeste, Daiga M.; Seeman, Philip; Coscina, Donald V. Seeman: Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **Relation between brain catecholamine receptors and dopaminergic stereotypy in rat strains.** European Journal of Pharmacology. 69(4):465-470, 1981.

A relation between D2 dopamine-neuroleptic receptor density and behavioral responsiveness to the dopamine agonist apomorphine was determined in rats. Apomorphine elicited significantly more stereotypy in male F344 rats than in male rats of the Buffalo (BUFF) strain. Studies of 3H-spiperone binding revealed the presence of 34% more D2-receptors in the striatum and 50% more D2-receptors in the olfactory tubercle of F344 rats than in BUFF rats. Alpha2-adrenoceptors in the frontal cortex were 20% higher in the F344 rats than in BUFF rats. Alpha1-adrenoceptors did not differ across strains. 28 references. (Author abstract modified)

004132 Herling, Seymore; Coale, Edward H., Jr.; Valentino, Rita J.; Hein, David W.; Woods, James H. M6311 Medical Science Building I, Dept. of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109 **Narcotic discrimination in pigeons.** Journal of Pharmacology and Experimental Therapeutics. 214(1):139-146, 1980.

In White Carneaux pigeons trained to discriminate intramuscular injection of 10mg/kg morphine from saline in a keypeck task with food reward, codeine (32mg/kg) and the methionine enkephalin analogue FK-33824 (3.2mg/kg) produced stimulus control of behavior comparable to that of morphine. The kappa-agonists ketazocine (10mg/kg) and ethylketazocine (3.2mg/kg) and the N-furyl benzomorphans, UM-909 (10mg/kg) and UM-1072 (1.0mg/kg), produced morphine appropriate responding. Naltrexone (1.0mg/kg) completely antagonized the stimulus control of behavior exerted by morphine and ethylketazocine. The mixed narcotic agonists/antagonists cyclazocine and SKF-10,047 and the nonnarcotic drugs pentobarbital, dextrorphan, ketamine, UM-1046, and clonidine, produced predominantly saline appropriate responding. Pentazocine, nalorphine, and meperidine produced responding intermediate between those appropriate for morphine and for saline. Results are discussed in relation to discriminative effects of narcotic drugs in other species. 37 references. (Author abstract modified)

004133 Herling, Seymore; Woods, James H. M6311 Medical Science Building I, Dept. of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109 **Chlorpromazine effects on cocaine-reinforced responding in rhesus monkeys: reciprocal modification of rate-altering effects of the drugs.** Journal of Pharmacology and Experimental Therapeutics. 214(2):354-361, 1980.

The effects of intramuscular injections of chlorpromazine were studied in rhesus monkeys whose lever-press responding was maintained under a second-order, fixed-interval, fixed-ratio schedule of food or cocaine reinforcement. When the dose per injection of cocaine was small, chlorpromazine produced similar dose related decreases in responding maintained by either cocaine or food. As the dose of cocaine was increased, the effects of chlorpromazine were attenuated, suggesting a dose related antagonism by self-injected cocaine of the rate decreasing effects of chlorpromazine. The behavioral effects of combinations of cocaine and chlorpromazine appear to involve a reciprocal antagonism of the rate modifying effects of the drugs. 25 references. (Author abstract modified)

004134 Herling, Seymore; Woods, James H. Dept. of Pharmacology, University of Michigan, Ann Arbor, MI 48109 **Discriminative stimulus effects of etorphine in rhesus monkeys.** Psychopharmacology. 72(3):265-267, 1981.

In two rhesus monkeys trained to discriminate etorphine (0.001mg/kg) from saline, administrations of etorphine (0.0001 to 0.0018mg/kg), meperidine (0.1 to 1.0mg/kg), morphine (0.1 to 3.2mg/kg), and codeine (0.3 to 3.2mg/kg) produced dose related increases in the percentage of responses on the etorphine appropriate lever. Ethylketazocine, pentazocine, and N-allylnormetazocine produced responses primarily on the saline appropriate lever. Results indicate that etorphine-like narcotics have discriminative stimulus effects in rhesus monkeys that can be distinguished from those of narcotics with nonmorphine-like actions. 15 references. (Author abstract modified)

004135 Hodge, Gordon K.; Boyeson, Michael G.; Linn, Richard T. Dept. of Psychology, University of New Mexico, Albuquerque, NM 87131 **Dopaminergic agonists differentially affect open-field activity of rats with A10 lesions.** Psychopharmacology. 73(1):39-42, 1981.

The differential effects on open-field behavior of rats with A10 lesions caused by dopaminergic agonists (apomorphine, d-amphetamine, or methylphenidate) were studied. Bilateral radio frequency lesions of area A10 in rats failed to affect spontaneous open-field behavior over a 1 month postoperative period. When injected with 1mg/kg of apomorphine, however, experimental rats more than doubled their activity as compared to the response of sham operated control Ss. In contrast, no difference between the two groups of animals was observed in terms of increased activity following 3mg/kg of either d-amphetamine or methylphenidate. These results are consistent with previous work indicating the involvement of ventromedial mesencephalic dopamine somata in the control of locomotor activity. The data suggest, however, that systems in addition to the dopaminergic mesolimbic projection are responsible, in part, for the hyperactivity elicited by d-amphetamine or methylphenidate. 20 references. (Author abstract modified)

004136 Holtzman, Stephen G. Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Phencyclidine-like discriminative effects of opioids in the rat.** Journal of Pharmacology and Experimental Therapeutics. 214(3):614-619, 1980.

Possible commonalities in the discriminative stimulus properties of phencyclidine (PCP) and opioids were investigated in rats trained to discriminate between i.p. injections of saline and 2.0mg/kg of PCP in a two choice, discrete trial avoidance paradigm. Tests of stimulus generalization were performed over an eightfold to 32fold range of doses with ketamine, a PCP analog, and eight opioids. Dose dependent and time dependent stimulus control of behavior comparable to that produced by 2.0mg/kg of PCP were produced by ketamine and the opioids cyclazocine, SKF 10,047, and dextrorphan. These drugs also produced orderly increases in responses during the interval between trials suggestive of a relationship between this effect and PCP-like stimulus control. In contrast, after ethylketocyclazocine, ketocyclazocine, pentazocine, and dextromethorphan trials were completed primarily on the saline appropriate lever and responding between trials did not change. Neither the PCP-like stimulus control of behavior nor the increased responding between trials produced by cyclazocine were prevented by pretreatment with naltrexone. These results provide further evidence that PCP and certain opioids share a common component of action that is probably mediated by neuronal substrates not usually associated with the activity of opioids. 35 references. (Author abstract modified)

004137 Horton, Roger; Anlezark, Gill; Meldrum, Brian. Meldrum: Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London SE5 8AF, England **Noradrenergic influences on sound-induced seizures.** Journal of Pharmacology and Experimental Theraeputics. 214(2):437-442, 1980.

Noradrenergic influences on sound-induced seizures were investigated. The preferential alpha2 noradrenergic agonists, clonidine, oxymetazoline, and UK 14,304 reduced the severity of audiogenic seizures in 19-day-old and 26-day-old DBA/2 mice. This protective effect could be diminished or reversed by alpha-2-noradrenergic antagonists such as yohimbine, piperoxan, or intracerebroventricular phentolamine. It is not reversed by the preferential alpha1 noradrenergic antagonist phenoxybenzamine. It is concluded that activation of a receptor pharmacologically similar to the peripheral alpha2 noradrenergic receptor protects against seizures in this epilepsy model. 49 references. (Author abstract modified)

004138 Igarashi, M.; Levy, J. K.; O-Uchi, T.; Homick, J. L. Dept. of Otorhinolaryngology and Communicative Sciences, Baylor College of Medicine, Houston, TX 77030 **Diazepam-induced ataxia in trotting squirrel monkeys.** Agressologie. 21(3):151-153, 1980.

The effect of diazepam on squirrel monkeys' gait was studied. Five squirrel monkeys who had been trained to trot on the center line of the squirrel monkey platform runway were injected with 2.0mg diazepam per kg of body weight. The platform test was repeated at 15 minutes, 1, 2, 3, 4, 5, and 24 hours after the injection. Results show that diazepam interfered with straight trotting by increasing lateral deviations. Because of diazepam's ability to produce ataxia, it is suggested that humans be cautious when performing motor tasks while under its influence. 9 references. (Journal abstract modified)

004139 Ikeda, Yasuo; Sasa, Masashi; Takaori, Shuji. Dept. of Pharmacology, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto 606, Japan **Selective effect of ethanol on the vestibular nucleus neurons in the cat.** Japanese Journal of Pharmacology. 30(5):665-673, 1980.

The effects of ethanol on neuronal activities in the lateral vestibular nucleus (LVN) and spinal trigeminal nucleus (STN) were investigated in cats. The LVN neurons were classified as monosynaptic, polysynaptic-I, and polysynaptic-II on the basis of latency to the first spike elicited by orthodromic vestibular nerve stimulation and antidromic vestibulospinal tract stimulation. Ethanol (0.2 to 1.6g/kg i.v.) dose dependently suppressed the orthodromic spike generation of monosynaptic and polysynaptic-II neurons. Mean spike numbers of monosynaptic and polysynaptic-II neurons were significantly decreased by ethanol doses greater than 0.4g/kg, but the polysynaptic-I neuron was unaffected by up to 0.8g/kg ethanol. Spike generation of the STN relay neurons and the interneuron elicited by trigeminal nerve stimulation was also unaltered by up to 0.8g/kg ethanol. 22 references. (Author abstract modified)

004140 Isaacson, Robert L.; Lanthorn, Thomas H. Dept. of Psychology, State University of New York, Binghamton, NY 13901 **Hippocampal involvement in the pharmacologic induction of withdrawal-like behaviors.** Federation Proceedings. 40(5):1508-1512, 1981.

Studies of the hippocampal involvement in the pharmacologic induction of withdrawal-like behaviors are described. Intracerebroventricular injection of nontoxic doses of kainic acid in rats produced behaviors similar to morphine withdrawal. Lesion of CA3 and CA4 abolished this response to kainic acid. The differential effects of CA3 and CA4 lesions on effects of various agents causing withdrawal-like behavior and challenge by naloxone and morphine may indicate that two neural circuits exist through which withdrawal-like behaviors are evoked. The hippocampal circuit is not directly involved in dependence, but may modulate withdrawal. 29 references. (Author abstract modified)

004141 James, Thomas A.; Starr, Michael S. Starr: Dept. of Pharmacology, School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, England **Rotational behaviour elicited by 5-HT in the rat: evidence for an inhibitory role of 5-HT in the substantia nigra and corpus striatum.** Journal of Pharmacy and Pharmacology. 32(3):196-200, 1980.

Unilateral intranigral microinjection of 5-hydroxytryptamine (5-HT) or 1-(1-((indol-3-yl)methyl)piperid-4-yl)-3-benzoylurea (Wy-25093), a selective inhibitor of 5-HT uptake, elicited ipsiversive circling and a fall in striatal dopamine (DA) turnover in male Wistar rats. Intranigral injection of methysergide or unilateral lesion of the raphe/nigral 5-HT pathway produced contraversive turning and increased DA turnover. Both types of behavior were accentuated by nialamide and attenuated by haloperiodol. Intracaudate injections of 5-HT or Wy-25093 provoked contraversive turning which was increased by nialamide and hyoscine, partially diminished by haloperidol, and antagonized by eserine. Intracaudate injections of methysergide-induced ipsiversive circling, which was potentiated by nialamide and eserine, depressed by hyoscine, and unaffected by haloperidol. Results suggest there is an inhibitory 5-HT/DA link in the substantia nigra and an inhibitory synapse between serotonergic and cholinergic neurons in the corpus striatum. 21 references. (Author abstract modified)

004142 Jarbe, T. U. C.; Sterner, U.; Hjerpe, C. University of Uppsala, Dept. of Psychology, P.O. Box 227, S-75104 Uppsala, Sweden **Conditioning of an interoceptive drug stimulus to different exteroceptive contexts.** Psychopharmacology. 73(1):23-26, 1981.

Two experiments showing that a pentobarbital versus saline discrimination can be differentially conditioned to different external contexts are described. In Experiment 1, rats differentiated two T-mazes (one water maze and one electrified maze). In Experiment 2, the external stimuli were the presence and absence of lights during training in the electrified T-maze. These experiments constitute the first examples where a single drug vs. nondrug discrimination has been conditioned to different external contexts requiring an opposite response pattern by the same animal. The data are in accordance with a stimulus interpretation of drug discrimination learning. 15 references. (Author abstract modified)

004143 Jensen, Robert A.; Messing, Rita B.; Spiehler, Vina R.; Martinez, Joe L., Jr.; Vasquez, Beatriz J.; McGaugh, James L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Memory, opiate receptors, and aging.** Peptides. 1(Suppl. 1):197-201, 1980.

Differences in retention of avoidance responses and in the opiate antagonist effect were investigated in young and F344 aged rats. Aged rats showed poorer retention of an inhibitory avoidance response, but showed better performance in an active avoidance response. The findings indicate that in some cases, the direction of the opiate antagonist effect created by naloxone administration depends upon age. With low footshock, naloxone either impairs or has no effect on retention in old Ss, but with high footshock, naloxone enhances the retention performance, indicating that age related changes in opioid systems may underly some behavioral differences between young and aged Ss. Opiate receptor bonding was then examined in vitro in various brain regions of young and old Ss. Analysis of dihydromorphine binding indicated that opiate receptor concentration in aged Ss is reduced in some brain regions, and that these changes are different in aged male and female Ss. Studies of in vivo bindings of opiate receptors yielded relationships between receptor changes and differences in response to footshock in the flinch jump test. It is concluded that age related alterations in brain opioid system may be involved in changes in learning and memory processes that occur with senescence. These results with animal models are seen as having relevance to studies of neural systems that may underly memory impairments in aged humans. 31 references. (Journal abstract modified)

004144 Jobe, Phillip C.; Ray, Tom B. Dept. of Pharmacology and Therapeutics, Louisiana State University School of Medicine, P. O. Box 33932, Shreveport, LA 71130 **Effects of norepinephrine and 5-hydroxytryptamine reuptake inhibitors on electrically-induced spinal cord seizures in rats.** Research Communications in Chemical Pathology and Pharmacology. 30(1):185-188, 1980.

In female Sprague-Dawley rats, the norepinephrine reuptake inhibitors nisoxetine and desipramine each exerted a suppressant effect on spinal cord seizures by decreasing the duration of tonic extension. In addition, desipramine increased the duration of tonic flexion and nisoxetine decreased the total duration of seizure. None of these seizure components was affected by citalopram, an inhibitor of 5-hydroxytryptamine reuptake. Results suggest that spinal cord noradrenergic neurons, but not serotonergic neurons, act as attenuators of convulsive activity. 10 references. (Author abstract modified)

004145 Jobe, Phillip C.; Woods, Thomas W.; Ray, Tom B. Dept. of Pharmacology and Therapeutics, Louisiana State University School of Medicine, Shreveport, LA 71130 **Effects of fluoxetine on electrically-induced spinal cord seizures in rats.** Research Communications in Chemical Pathology and Pharmacology. 30(1):189-192, 1980.

The effects of fluoxetine on electrically-induced spinal cord seizures were studied in female Sprague-Dawley rats. A 10mg/kg i.p. dose of fluoxetine had no effect on spinal cord seizures or on 5-hydroxytryptamine (5-HT) reuptake, measured by changes in 5-hydroxyindoleacetic acid (5-HIAA) content. However, a 20mg/kg dose significantly reduced 5-HIAA content without affecting seizure activity. Results indicate that 5-HT containing neurons in the spinal cord to do not modulate electrically-induced seizure activity. 5 references. (Author abstract modified)

004146 Jones, Jeffrey G.; Richter, Judith A. Dept. of Pharmacology, Indiana University School of Medicine, Indianapolis, IN 46223 **The site of action of naloxone in suppressing food and water intake in rats.** Life Sciences. 28(18):2055-2064, 1981.

The site of action of naloxone in suppressing food and water intake in rats was investigated by giving bilateral injections of 15mcg/rat of naloxone into the lateral ventricles of cannulated, food and water deprived rats. This treatment caused a significant decrease in food but not water intake. Equal doses of naloxone in the periphery did not produce behavioral changes. The data imply that naloxone exerts its effect on food intake at a central site. Subsequent experiments indicate that this central site of action is mediated by the vagus, and specifically by vagal efferents, since the effect was blocked by methylatropine. Results also suggest that naloxone's effect on water intake is mediated by a different mechanism than that involved with food intake. 39 references. (Author abstract modified)

004147 Joshi, Vinita V.; Balsara, Jehangir J.; Jadhav, Jagdish H.; Chandorkar, Arwind G. Dept. of Pharmacology, V. M. Medical College, Solapur (Maharashtra) I-413003, India **Effect of L-histidine and chlorcyclizine on apomorphine-induced climbing behaviour and methamphetamine stereotypy in mice.** European Journal of Pharmacology. 69(4):499-502, 1981.

Pretreatment with the histamine precursor L-histidine (850 and 1000mg/kg i.p.) or the H1-receptor blocker chlorcyclizine (25 and 50mg/kg i.p.) failed to modify apomorphine-induced climbing behavior in male albino mice. However, pretreatment with 850 or 1000mg/kg L-histidine antagonized stereotypy induced by methamphetamine. Pretreatment with 25mg/kg chlorcyclizine potentiated the methamphetamine stereotypy. 10 references. (Author abstract modified)

004148 Kamata, Katsuo; Okuyama, Shigeru; Kameyama, Tsutomu. Dept. of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Effects of analgesics and CNS-acting drugs on struggling following repetitive stimulation of the tail, and flexor reflex to a single stimulation of**

the sciatic nerve in rats. Japanese Journal of Pharmacology. 30(3):357-366, 1980.

The analgesic and muscle relaxant effects of several analgesics were evaluated in male Wistar rats. Struggling in response to repetitive stimulation of the tail was used as a measure of pain response, and the flexor reflex response to a single stimulation of the sciatic nerve was used as a measure of spinal reflex activity. The 50% inhibitory doses for struggling and flexor reflex were (in mg/kg i.p.): morphine, 3.30 and 6.60, respectively; codeine, 12.80 and 24.00; pentazocine, 7.80 and 12.20; indomethacin, 4.60 and no effect; aspirin, 94.00 and no effect; baclofen, 1.04 and 2.20; chlorpromazine, 2.45 and 0.75; diazepam, 0.45 and 0.86; and mephenesin, 36.00 and 32.00. 22 references. (Author abstract modified)

004149 Kamei, C.; Oka, M.; Masuda, Y.; Yoshida, K.; Shimizu, M. Shimizu: Dept. of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Suita-Shi, Osaka 564, Japan **Effects of 3-sulfamoylmethyl-1,2-benzisoxazole (AD-810) and some antiepileptics on the kindled seizures in the neocortex, hippocampus and amygdala in rats.** Archives Internationales de Pharmacodynamie et de Therapie. 249(1):164-176, 1981.

The effects of 3-sulfamoylmethyl-1,2-benzisoxazole (AD-810) on kindled seizures in the neocortex, hippocampus, and amygdala of male Wistar rats were compared with those of clinically proven antiepileptics. Kindled seizures developed more rapidly in the amygdala than in the hippocampus and neocortex. Phenobarbital, carbamazepine, dipropylacetate, phenytoin, and diazepam depressed neocortical kindled seizures. Phenobarbital and carbamazepine depressed hippocampal kindled seizures, but phenytoin and diazepam had little effect. Phenobarbital and diazepam markedly depressed amygdaloid kindled seizures, but phenytoin, carbamazepine, and dipropylacetate had only weak effects. AD-810 resembled carbamazepine, showing a depressant effect on neocortical and hippocampal kindled seizures but not amygdaloid kindled seizures. 16 references. (Author abstract modified)

004150 Kanarek, Robin B.; Ho, Lap; Meade, Robert G. Dept. of Psychology, Tufts University, Medford, MA 02155 **Sustained decrease in fat consumption produced by amphetamine in rats maintained on a dietary self-selection regime.** Pharmacology Biochemistry and Behavior. 14(4):539-542, 1981.

Total daily caloric intake and dietary self-selection of protein, fat, and carbohydrate were examined in female Sprague-Dawley rats given d-amphetamine sulfate (0.5, 1.0, or 2.0mg/kg i.p.). Animals had access to nutrients for a 6 hour period each day, and food intakes were measured 2 hours after food presentation and at the end of the 6 hour period. Dose related decreases in caloric intakes in animals maintained on a standard laboratory diet were similar to those in rats maintained on the dietary self-selection regime. In the latter group, protein and carbohydrate intakes were suppressed by all three drug doses during the initial 2 hour measurement period but returned to control values by the end of the 6 hour period. Fat intake was initially suppressed by amphetamine and remained suppressed throughout the 6 hour measurement period. 14 references. (Author abstract modified)

004151 Karczmar, Alexander G.; Kindel, Gisela H. Dept. of Pharmacology and Therapeutics, Loyola University Medical Center, Maywood, IL 60153 **Acetylcholine turnover and aggression in related three strains of mice.** Progress in Neuro-Psychopharmacology. 5(1):35-48, 1981.

Brain acetylcholine (ACh) turnover and brain ACh and choline levels were determined in CF-1, C57BL/6 By, and Balb-c-By mice after mild footshock and isolation. Baseline levels of ACh and choline were lower in aggregated Balb-c-By mice than in the two other strains. ACh turnover in aggregated CF-1 mice was at least twice as high as that in the other two strains. The effects of shock, isolation, or shock combined with isolation on brain levels of ACh and choline were inconsistent. ACh turnover was significantly decreased by shock or isolation in CF-1 mice, but not in the other two strains. CF-1 mice were significantly more aggressive than the other two strains after isolation, shock, or both. Results are discussed in relation to the aggressive effect of muscarinic drugs and the antiaggressive effect of atropinic drugs. 38 references. (Author abstract modified)

004152 Katz, Jonathan L. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115 **Second-order schedules of intramuscular cocaine injection in the squirrel monkey: comparisons with food presentation and effects of d-amphetamine and promazine.** Journal of Pharmacology and Experimental Therapeutics. 212(3):405-411, 1980.

The effects of d-amphetamine and promazine on second-order schedules of intramuscular cocaine injection in the squirrel monkey were investigated. Squirrel monkeys pressed a key under second-order schedules of cocaine injection with a single i.m. injection at the end of a daily experimental session. A second group of squirrel monkeys responded under comparable schedules of food presentation. Under one schedule, each 10th response produced a 1 second visual stimulus; completion of the first fixed-ratio requirement after 30 minutes had elapsed produced the stimulus and either a cocaine injection or food presentation. Under another schedule, the first response after each 3 minutes had elapsed produced a 1 second visual stimulus; completion of the 10th fixed-interval requirement produced the stimulus and either a cocaine injection or food presentation. When saline was substituted for cocaine or when food presentations were omitted, response rates decreased; increasing the dose of cocaine or the amount of food beyond some minimum increased response rates. Administrations of d-amphetamine before sessions generally increased average response rates under both second-order schedules regardless of whether food or cocaine maintained responding. With cocaine injections confined to the end of the session, d-amphetamine and promazine affected cocaine maintained and food maintained responding in a similar manner. 34 references. (Author abstract modified)

004153 Katz, R. J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Possible muscarinic-cholinergic mediation of patterned aggressive reflexes in the cat.** Progress in Neuro-Psychopharmacology. 5(1):49-56, 1981.

In a study of cholinergic influences on attack behavior, patterned aggressive reflexes (head turning, biting, and paw striking) elicited by hypothalamic stimulation were examined in female cats. Cholinergic stimulation by intraventricular injection of arecoline facilitated the three reflexes, and cholinergic blockade by intraventricular injection of scopalamine inhibited the reflexes. Results suggest that cholinergic muscarinic receptors may mediate terminal (consummatory) behaviors in aggressive syndromes. 13 references. (Author abstract modified)

004154 Katz, R. J.; Schmaltz, K. Mental Health Research Institute, Dept. of Psychiatry, University Of Michigan Medical Center, Ann Arbor, MI 48109 **Reduction in opiate activation after chronic electroconvulsive shock -- possible role for endorphins in the behavioral effects of convulsive shock treatment. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-31588, 1980. 10 p.

To study the possible role of endorphins in the behavioral effects of convulsive shock treatment, group housed adult male Sprague-Dawley rats received a series of four exposures to shock therapy or equivalent handling without shock (sham treatment). Twenty four hours after the final treatment, Ss were given vehicle or one of two doses of morphine intraperitoneally, and motor activity was assessed by remote sensing for 60 minutes. A significant shift of the normal dose response curve towards the right was seen after electroshock. This may point to cross-tolerance between electroshock and opiates upon this behavioral measure. The results are consistent with the hypothesis that endorphins may mediate certain aspects of electroshock. Some biochemical aspects of depression and its treatment are considered. 13 references. (Author abstract modified)

004155 Katz, R. J.; Schmaltz, K. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Behavioral interactions between opiate and antiepileptic drugs in the mouse.** Neuropharmacology. 20(4):375-379, 1981.

The effects of sodium valproate, trimethadione, and taurine on behavioral activation induced by opiate or opioid compounds were studied in male Swiss-Webster mice. Morphine-induced increases in activity were facilitated by sodium valproate and trimethadione, even though these drugs inhibited activity when given alone. Taurine had an inhibitory effect when given alone but did not interact with morphine. The effects of the three anticonvulsants on activation produced by central administration of D-ala2-leu-enkephalinamide were similar to their effects on responses to morphine. Results demonstrate a behavioral interaction between opiate and anticonvulsant drugs. 8 references. (Author abstract modified)

004156 Katz, R. J.; Schmaltz, K. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Contribution of social factors to opiate-induced activation in the mouse.** Neuropharmacology. 20(4):381-383, 1981.

Adult male Swiss-Webster mice habituated singly or in groups of two, three, or four to test cages were injected with 25mg/kg or 50mg/kg morphine sulfate or vehicle. Morphine increased behavioral activity and induced stereotyped forward locomotion. This motor response was disproportionately enhanced by the presence of conspecifics. Results suggest that morphine-induced activation of grouped animals reflects individual activation responses as well as social factors. 8 references. (Author abstract modified)

004157 Kendall, D. A.; Fox, D. A.; Enna, S. J. Enna: Dept. of Neurobiology and Anatomy, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **Effect of gamma-vinyl GABA on bicuculline-induced seizures.** Neuropharmacology. 20(4):351-355, 1981.

Male ICR mice were treated with the GABA transaminase inhibitor gamma-vinyl GABA (GVG) 4 or 24 hours before challenge with convulsant doses of picrotoxin, bicuculline, strychnine, or isoniazid. Brain GABA levels were 15 times higher than control 4 hours after 1500mg/kg GVG, and seizures induced by all the convulsants except bicuculline were attenuated significantly. In contrast, 24 hours after 1500mg/kg GVG when brain GABA was seven times higher than control, significant protection against bicuculline-induced seizures was observed while protection against the other agents had diminished greatly. Bicuculline-induced seizures were reduced 4 hours after a 1000mg/kg dose of GVG, which also yielded a sevenfold increase in brain GABA content. 19 references. (Author abstract modified)

004158 Kilpatrick, Ian C.; Starr, Michael S. Starr: Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Involvement of dopamine in circling responses to muscimol depends on intranigral site of injection.** European Journal of Pharmacology. 69(4):407-419, 1981.

The intensity, direction, and dopamine dependence of circling behavior were determined in male Wistar rats after stereotaxic injections of 40ng muscimol (in 0.2mcl over 3 minutes) into various regions of the substantia nigra (SN). Weak, haloperidol sensitive, ipsilateral postural or locomotor asymmetries were obtained from the rostral SN zona compacta (SNC), whereas robust, contraversive rotational behavior was elicited from the SN zona reticulata (SNR) and caudal SNC. Turning evoked from the central SNR was attenuated markedly by pretreatment with haloperidol (0.1mg/kg i.p.) or pimozide (0.25mg/kg i.p.) or 6-hydroxydopamine lesions of the nigrostriatal dopaminergic pathway. Turning elicited from the lateral and ventral positions of the SNR was weakened significantly and not susceptible to dopaminergic blockade. Lower circling rates were obtained when the SNR injections were made rapidly (in 30 seconds), in a large volume (0.5mcl), or at a supramaximal dose (400ng). 50 references. (Author abstract modified)

004159 Koek, Wouter; Slangen, Jef L. Dept. of Psychology, University of Utrecht, Sorbonnelaan 16, NL-3508 TB Utrecht, The Netherlands **Habituation of the the head-poke response: effects of an amphetamine-barbiturate mixture, PLG and fenfluramine.** Psychopharmacology. 72(3):251-256, 1981.

A mixture of amphetamine and amylobarbitone attenuated the habituation of exploratory behavior (head poke response) without influencing locomotion and rearing in male Wistar rats. The oxytocin fragment Pro-Leu-Gly-NH2 (PLG) increased locomotor activity without altering the course of habituation of the head poke response. The amphetamine/amylobarbitone mixture did not influence the stimulus specificity of habituation of the head poke response. Fenfluramine increased the effects of stimulus change on the head poke response without altering habituation of the response. Results indicate that exploration can be dissociated pharmacologically from locomotor activity and that habituation of exploratory behavior can be dissociated pharmacologically from stimulus specificity of habituation. 10 references. (Author abstract modified)

004160 Kornetsky, Conan; Esposito, Ralph U. Boston University School of Medicine, Division of Psychiatry, Laboratory of Behavioral Pharmacology, 80 E. Concord St., Boston, MA 02118 **Reward and detection thresholds for brain stimulation: dissociative effects of cocaine.** Brain Research. 209(2):496-500, 1981.

The effects of cocaine on both rewarding and detection thresholds for intracranial stimulation to the same brain sites in the same animals were determined. The drug caused a dissociation in effects on the two types of brain stimulation. Detection threshold was elevated at doses of cocaine that lowered the reward threshold. If it is assumed that the detection threshold represents a functionally significant measure of sensitivity, then these data may indicate that the action of the drug on reinforcement levels is mediated at a site(s) other than the locus of stimulation. These and other results argue against a simple relationship between localization of drug action and the site of electrode tips. 10 references. (Author abstract modified)

004161 Kryzhanovskiy, G. N.; Aliyev, M. N. Lab. obshchey patologii nervnoy sistemy, Institut obshchey patologii i patofiziologii AMN SSSR, Moskva, USSR **/The pathogenesis of stereotypic behavior./** K patogenezu stereotipnogo povedeniya.

Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(9):1347-1355, 1979.

The pathogenesis of stereotypic behavior was studied in rats using tetanus toxin, haloperidol, GABA, penicillin, picrotoxin, seduxen, aminalon, and lithium. Results show that the pathogenesis of stereotypic behavior is a chain process, consisting of a series of stages. The first stage is the disturbance of GABA inhibitory control over dopamine secretion from the terminals of dark substance dopaminergic neurons terminating in the caudate nuclei. The second is the disinhibition of the hyperactivity of the dopamine mechanism of the caudate nuclei. The third is a change in the activity of the cholinergic neurons of the caudate nuclei under the influence of dopamine. Stereotypic behavior can occur when corresponding changes take place in only the last two stages of this process. These results also show that the condition of the serotonin and noradrenaline neuromediator systems in the caudate nuclei can change stereotypic behavior in animals. 48 references.

004162 Kryzhanovskiy, G. N.; Aliyev, M. N. Lab. obshchey patologii nervnoy sistemy, Institut obshchey patologii i patologicheskoy fiziologii AMN SSSR, Moskva, USSR **/The complex specific pathogenetic therapy of the stereotypic behavior syndrome (an experimental study)./** Kompleksnaya spetsificheskaya patogeneticheskaya terapiya sindroma stereotipnogo povedeniya (eksperimental'noye issledovaniye). Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(2):225-231, 1980.

The pathogenetic treatment of the stereotypical behavior syndrome in rats is discussed based on the findings of a pharmacological study. This syndrome was reproduced by destroying GABAergic control over the dopamine system in both caudate nuclei through microinjections of tetanus toxin into the rostral part of the neostriatum. Combined administration of lithium chloride, diazepam, and haloperidol in doses producing the minimal effect when the drugs were used alone evokes long-term inhibition of practically all signs of the stereotypic behavior syndrome. The results are discussed with regard to the role of hyperactive determinant structures in CNS pathology. The effect of dopamine on stereotypical behavior in animals is due to its direct effect on the restoration of disturbed inhibitory mechanisms in the determinant structure, its effect on the level of the neurons forming mediator inputs to the caudate nuclei, and also its effect on the system of output from the determinant structure to the designation stations. Haloperidol prevents dopamine hyperactivity in stereotypical behavior, blocking the catecholamine receptors. Lithium suppresses the activity of the catecholaminergic systems. 32 references. (Journal abstract modified)

004163 Kryzhanovskiy, G. N.; Aliyev, M. N. Inst. of General Pathology and Pathological Physiology, Baltiyskaya 8, Moscow 125315, USSR **The stereotyped behavior syndrome: a new model and proposed therapy.** Pharmacology Biochemistry and Behavior. 14(3):273-281, 1981.

Bilateral microinjections of tetanus toxin (TT), penicillin, or picrotoxin into the rostral part of the caudate nucleus of male white rats (to induce local impairment of inhibitory GABAergic mechanisms) produced a stereotyped behavior syndrome. This syndrome was suppressed by haloperidol (i.p.) in a dose dependent manner. Stereotyped behavior induced by TT was suppressed by bilateral microinjection of GABA into the rostral part of the caudate nucleus. Lithium chloride and diazepam, administered i.p., were also able to suppress the stereotyped behavior syndrome. Combined application of lithium, diazepam, and haloperidol in minimally effective doses resulted in more complete and longer lasting supression of the syndrome than separate use of these drugs. 46 references. (Author abstract modified)

004164 Kulkarni, S. K.; Arzi, A.; Kaul, P. N. Dept. of Pharmaceutical Sciences, Panjab University, Chandigarh-160014, India **Modification of drug-induced catatonia and tremors by quipazine in rats and mice.** Japanese Journal of Pharmacology. 30(2):129-135, 1980.

The serotonin agonist quipazine counteracted some of the drug-induced symptoms of pseudoparkinsonism in male Sprague-Dawley rats and Swiss-Webster mice. Quipazine prouced a dose dependent inhibition of the catatonia induced by perphenazine and partially blocked tremors induced by nicotine and tremorine. Harmine-induced tremors were potentiated by quipazine. Studies of the effects of quipazine combined with other antiparkinson agents such as scopolamine, diphenhydramine, and amatadine indicated that cholinergic, dopaminergic, and histaminergic receptors play an important role in the manifestation of parkinsonian symptoms. 24 references. (Author abstract modified)

004165 Kuribara, Hisashi; Tadokoro, Sakutaro. Division for Behavior Analysis, Behavior Research Institute, School of Medicine, Gunma University, 3-39-22 Showa-machi, Maebashi 371, Japan **Schedule dependent change of punished responding after diazepam in rats.** Japanese Journal of Pharmacology. 30(2):264-268, 1980.

The effect of diazepam on conditioned response suppression was studied in male Wistar rats on a fixed-ratio 30 schedule of food or water reinforcement. Results indicated that diazepam specifically increased punished responding, without affecting discriminative ability. 13 references.

004166 Lazarova, M.; Roussinov, K.; Kleinrok, Z.; Rajtar, G. Institute of Physiology, Bulgarian Academy of Sciences, acad. G. Bonchev st. bl. 1, 1113 Sofia, Bulgaria **On some relationships between GABA-ergic and 5-HT-ergic mechanisms in pentylenetetrazol convulsive-seizure reactions.** Agressologie. 21(5):253-257, 1980.

The effect of various drugs in controlling pentylenetetrazol induced seizures in rats and the relationship between the GABA-ergic and 5-HT-ergic systems and these seizures were studied. Various doses of GABA, 5-HTP, aminooxyacetic acid (AOAA), para-chlorophenylalanine (PCPA), and di-n-propylacetate (DPA) were injected intraperitoneally before subcutaneous injection of 80mg/kg pentylenetetrazol (PTZ). Results show that in doses which markedly increase the brain level of GABA, DPA 250mg/kg, AOAA 20mg/kg, GABA 1000mg/kg, and 5-HTP 200mg/kg inhibited the seizure reactions, but PCPA increased the seizures. A combination of GABA, DPA, or AOAA with 5-HTP increased the inhibitory effect. GABA and GABA-ergic agents reverse the seizure increasing effect of PCPA. These results suggest that the GABA-ergic and 5-HT-ergic systems exert a synergic, inhibitory effect on the PTZ convulsive seizure reactions. Activation of the GABA-ergic system (by increasing the brain level of GABA) could functionally compensate the PCPA decreased activity of the 5-HT-ergic system. 23 references. (Author abstract modified)

004167 Lerer, B.; Ebstein, R. P.; Felix, A.; Belmaker, R. H. Belmaker: Jerusalem Mental Health Center - Ezrath Nashim, P.O. Box 140, Jerusalem, Israel **Lithium amelioration of reserpine-induced hypoactivity in rats.** International Pharmacopsychiatry. 15(6):338-343, 1980.

The effects of lithium on hypoactivity induced by moderate and high doses of reserpine were studied in rats. Oral lithium pretreatment for 19 days significantly prevented the behavioral immobility induced by moderate doses of reserpine. High doses of reserpine overwhelmed the lithium effect. The data confirm previous results that lithium pretreatment can prevent the depressant effects of biogenic depletion in mammals, extend such findings from mice to rats, and show that the effect is unlikely to be a transient nonspecific lithium effect. Development of a simple and specific behavioral test of lithiumlike activity in animals could allow for screening and possible development of new lithiumlike compounds. 10 references. (Author abstract modified)

004168 Loscher, W. Lab. of Pharmacology and Toxicology, School of Veterinary Medicine, Free University Berlin, Koserstrasse 20, D-1000 Berlin 33, West Germany **Anticonvulsant activity of metabolites of valproic acid.** Archives Internationales de Pharmacodynamie et de Therapie. 249(1):158-163, 1981.

The effects of eight metabolites of valproic acid (VPA) on the thresholds for maximal electroconvulsion and pentetrazole convulsions were tested in male NMRI mice. All the metabolites significantly elevated the convulsive thresholds, but none was as potent as VPA itself. Results suggest that VPA itself is responsible for more than 80% of the antiepileptic effect of chronic VPA therapy in humans. 10 references. (Author abstract modified)

004169 Lucot, James B.; Horwitz, Joel; Seiden, Lewis S. Seiden: Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th St., Chicago, IL 60637 **The effects of p-chloroamphetamine administration on locomotor activity and serotonin in neonatal and adult rats. (Unpublished paper).** Research Report, NIMH Grant 5K05-MH-10562, 1979. 31 p.

The effects of p-chloroamphetamine (PCA) administration on locomotor activity and serotonin were investigated in neonatal and adult rats to determine the nature of the behavioral consequences of this drug. Administration on days 9 or 12 of life heightened the peak in locomotor activity that normally occurs about day 15. Administration on day 12 also shifted the occurrence of the peak to a later age. Administration at later ages produced increases in locomotor activity when first measured on the day after the injection, but not thereafter. The increases in locomotor activity in pups were obtained after depletions of serotonin that produced no effects on locomotion in adults. In adults, a small decrease in locomotor activity resulted at the highest dose, and the decrease resulted from an enhancement of the normal decline in locomotor activity as the 1 hour session progressed. Pups were uniformly active throughout the session and PCA produced no effect on the distribution of activity. Administration to pups produced an age dependent decrease in serotonin levels, but administration on day 24 did not produce as great a permanent depletion as did administration in adults. Examination of the short-term effects in 12-day-old Ss revealed a large initial depletion of serotonin, followed by a rapid recovery in the brainstem and diencephalon and a more gradual recovery in the caudate and telecephalon. There was a good correspondence in adults between serotonin levels and locomotor activity. In pups, the correspondence was less clear. 23 references. (Author abstract modified)

004170 Lukas, Scott E.; Moreton, J. Edward; Khazan, Naim. Moreton: Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, 636 W. Lombard St., Baltimore, MD 21201 **Effects of levo-alpha-acetylmethadol (LAAM) on morphine self-administration in the rat.** Psychopharmacology. 73(1):12-16, 1981.

The effects of levo-alpha-acetylmethadol (LAAM) on morphine self-administration in the rat were investigated. Rats bearing cerebrocortical electrodes for recording EEG were rendered tolerant to and physically dependent on morphine and subsequently trained to self-administer morphine through a chronic intravenous cannula. Once morphine intake had stabilized, LAAM was administered noncontingently via a chronic intragastric (IG) cannula as a single daily dose of either 1mg/kg or 4mg/kg. These morphine self-administering rats were maintained on daily LAAM treatment for 12 consecutive days. Analysis of the patterns of lever pressing, morphine self-injections, and sleep/awake behavior revealed that daily IG administration of LAAM effectively suppressed morphine self-administration. The dose related reduction in morphine self-administration occurred in the absence of overt signs of narcotic withdrawal, behavioral toxicity, or disruption of sleep/awake behavior in these rats. Termination of LAAM maintenance resulted in a gradual return of lever pressing and morphine intake to preLAAM levels. 36 references. (Author abstract modified)

004171 Lyness, W. H.; Moore, K. E. Dept. of Pharmacology and Therapeutics, Texas Tech. University School of Medicine, Lubbock, TX 79430 **Destruction of 5-hydroxytryptaminergic neurons and the dynamics of dopamine in nucleus accumbens septi and other forebrain regions of the rat.** Neuropharmacology. 20(4):327-334, 1981.

The effects of 5,7-dihydroxytryptamine (5,7-DHT) induced destruction of 5-hydroxytryptamine (5-HT) neurons on spontaneous and drug stimulated locomotor activity were studied in male Sprague-Dawley rats. Injection of 5,7-DHT into the lateral cerebral ventricle of rats pretreated with desipramine reduced the levels of 5-HT but not norepinephrine or dopamine (DA) levels in the forebrain regions. Bilateral injections of 5,7-DHT into the nucleus accumbens septi (NAS) of desipramine pretreated rats selectively depleted 5-HT only from the NAS. In both groups of 5-HT depleted animals, exploratory locomotor activity and locomotor stimulation induced by d-amphetamine or apomorphine were enhanced. The behavioral changes observed after destruction of 5-HT nerve terminals were not associated with changes in the activity of the major ascending dopaminergic systems. 38 references. (Author abstract modified)

004172 Marangos, Paul J.; Martino, Andrea M.; Paul, Steven M.; Skolnick, Philip. Clinical Psychobiology Branch, NIMH, Building 10, Room 4S239, 9000 Rockville Pike, Bethesda, MD 20205 **The benzodiazepines and inosine antagonize caffeine-induced seizures.** Psychopharmacology. 72(3):269-273, 1981.

The effects of benzodiazepines and purines on caffeine induced seizures were examined in male C3H/HEN mice. Seizures induced by caffeine were qualitatively indistinguishable from those induced by pentylenetetrazol (PTZ), and pretreatment with low doses of caffeine potentiated PTZ induced seizures. Benzodiazepines inhibited caffeine induced seizures with a rank order of potency that parallels their affinities for the CNS benzodiazepine receptor in vitro. Inosine, a purine that acts as a competitive inhibitor of 3H-diazepam binding in vitro, antagonized caffeine induced seizures; 7-methyl-inosine, a purine that lacks receptor binding inhibitory activity, had no effect on seizures. Results suggest that caffeine may exert some of its effects at the level of the benzodiazepine receptor and that purinergic modulation of benzodiazepine receptor status may be involved in seizure generation. 26 references. (Author abstract modified)

004173 Marcais, Helene; Bonnet, Jean Jacques; Costentin, Jean. Lab. de Pharmacodynamie & Physiologie, UER de Medecine & Pharmacie de Rouen, Ave. de l'Universite, F-76800 Saint Etienne du Rouvray, France **Evidence for sedative effects of low doses of morphine in mice involving receptors insensitive to naloxone.** Life Sciences. 28(24):2737-2742, 1981.

Evidence for sedative effects of low doses of morphine in mice involving receptors insensitive to naloxone is described.

Low doses of morphine decrease in a dose dependent manner spontaneous climbing behavior in mice. This effect is not modified by administration of naloxone at doses up to 1.25mg/kg. These morphine doses do not modify the locomotor activity but, when they are associated with naloxone, an obvious inhibition occurs. In rats, a hyperactivity follows the akinesia produced by a morphine administration. This hyperactivity is changed into a significant hypokinesia when the animals are treated with naloxone. These results might reveal a dual effect of low doses of morphine, the excitatory effect of morphine being antagonized by naloxone whereas no action on the sedative effect is observed. 16 references. (Author abstract modified)

004174 Mashkovskiy, M. D.; Andrejeva, N. I. Laboratory of Pharmacology, All-Union Chemical-Pharmaceutical Research Institute, Zubovskaya ul. 7, Moskva, USSR **Pharmacological properties of 2,3,3a,4,5,6-Hexahydro-8-methyl-1H-pyrazino(3,2,1-j,k) carbazol hydrochloride (pirlindole), a new antidepressant.** Arzneimittel-Forschung. 31(1):75-79, 1981.

The pharmacological properties are discussed of 2,3,3a,4,5,6-hexahydro-8-methyl-1H-pyrazino(3,2,1-j,k)carbazol hydrochloride (pirlindole), which is one of the more effective pyrazincindole derivatives that have been synthesized. Data are provided for the following experimental parameters concerning pirlindole: acute toxicity; antagonism to reserpine induced hypothermia and antagonism of tetrabenazine induced ptosis in mice; potentiation of d,l-amphetamine induced stereotyped behavior in rats; influence on L-dopa induced hypothermia and influence on apomorphine induced hypothermia in mice; potentiation of 5-HTP induced head twitch in mice; potentiation of tryptamine induced clonic seizures in the rat; effects on adrenaline, noradrenaline, tryptamine, and serotonin hypertensive response in anesthetized dogs; influence on oxotremorine induced hypothermia in mice; effect on barbiturate sleeping time in rats; effects on blood pressure of anesthetized cats; inhibition of MAO activity; and effect on noradrenaline uptake in the isolated rat's heart and on H77/77 uptake in noradrenaline neurons. Pirlindole was found to: antagonize the depressant effects of reserpine and tetrabenazine; potentiate the central effects of amphetamine and L-dopa; enhance the head twitch effect of 5-hydroxytryptophan; enhance the effects of noradrenaline, adrenaline, serotonin, and tyramine on blood pressure; enhance the hypertensive and tremor activities of tryptamine; inhibit the neuronal uptake of noradrenaline; and exert reversible, short lasting anti-MAO activity. Pirlindole does not possess anticholinergic activity, and clinical trials have shown pirlindole to be effective as an antidepressant drug. 20 references. (Journal abstract modified)

004175 McGuire, Patricia S.; Seiden, Lewis S. Seiden: University of Chicago, Dept. of Pharmacological and Physiological Sciences, 947 E. 58th St., Abbott Hall, Chicago, IL 60637 **The effects of tricyclic antidepressants on performance under a differential-reinforcement-of-low-rates schedule in rats.** Journal of Pharmacology and Experimental Therapeutics. 214(3):635-641, 1980.

The effects of tricyclic antidepressants on performance under a differential reinforcement of low rates schedule were investigated in rats. Doses of 2.5mg/kg to 10.0mg/kg of imipramine and desmethylimipramine decreased response rate and increased reinforcement rate. The interresponse time (IRT) distributions at these doses showed a suppression of IRTs shorter than 18 seconds and an increase in IRTs longer than 18 seconds. Higher doses of imipramine and desmethylimipramine decreased response rate as well as reinforcement rate. To determine whether the decrease in response rate and increase in reinforcement rate seen with imipramine and desmethylimipramine was related to their anticholinergic properties, scopolamine, a cholinergic blocking agent, was also tested. Unlike the other drugs, scopolamine increased response rate, decreased reinforcement rate, and increased IRTs shorter than 18 seconds. 33 references. (Author abstract modified)

004176 McKearney, James W. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Individual differences in effects of tricyclic antidepressants and anticholinergic drugs on operant behavior in the squirrel monkey.** Life Sciences. 28(18):2049-2054, 1981.

Individual differences in the effects of tricyclic antidepressants and anticholinergic drugs on operant behavior in the squirrel monkey were investigated. Amitriptyline was the most potent of the drugs studied, and nortriptyline, imipramine, chlorimipramine, and desmethylimipramine produced increases at higher doses. There was a close correspondence between the effects of amitriptyline and those of atropine in individual Ss. The monkeys showing increases in responding with amitriptyline also showed the most marked increases with atropine, and those showing no increases with amitriptyline also showed no increases with atropine. Interindividual differences in the effects of acutely administered tricyclic antidepressant drugs may be mediated by differential sensitivities of the monkeys to the antimuscarinic properties of these drugs. 14 references. (Author abstract modified)

004177 Messing, Rita B.; Jensen, Robert A.; Vasquez, Beatriz J.; Martinez, Joe L., Jr.; Spiehler, Vina R.; McGaugh, James L. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Opiate modulation of memory. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-12526, 1980. 23 p.

Evidence is presented that endogenous opioid systems are involved in memory storage processes. Research indicates that retention performance of rats is changed following posttraining administration of morphine, naloxone, or naltrexone. The memory modulatory effects of these drugs occurred only within a narrow dosage range, suggesting that these effects are mediated by mu-receptors. Additional findings indicate that: 1) the qualitative effects of these drugs on memory are highly time dependent; 2) the drugs all improve retention performance when given in equally divided doses immediately and 30 minutes after training; 3) a single administration of morphine immediately posttraining or of naloxone 30 minutes after training impairs rentention performance; 4) the similar effects of an opiate agonist and opiate antagonist on memory may be due to their common action of displacing endogenous peptides from receptor sites; 5) the time dependence of the drug effects may be caused by drug interactions with endogenous neurohumors which change as a function of time after a stressful experience; and 6) alternatively, a single neurochemical manipulation may result in different functional effects if it occurs at different times in the process of memory consolidation. 30 references. (Author abstract modified)

004178 Meyerson, Bengt J. Dept. of Medical Pharmacology, University of Uppsala, Biomedicum, Box 573, S-751 23 Uppsala, Sweden **Comparison of the effects of beta-endorphin and morphine on exploratory and socio-sexual behaviour in the male rat.** European Journal of Pharmacology. 69(4):453-463, 1981.

Intracerebral injection of 5mcg beta-endorphin or morphine in male Sprague-Dawley rats decreased exploratory activity and sociosexual approaches in tests with a sexually receptive female rat or a castrated male rat as stimulus object. At lower doses (0.5 to 1.0mcg), beta-endorphin had a selective inhibitory effect on copulatory behavior, but morphine caused general depression of both social and sexual behaviors. In contrast to morphine, beta-endorphin increased amicable social contacts at a dose (1mcg) that decreased sexual responses. Results suggest that beta-endorphin may influence mechanisms implicated in perception or interpretation of environmental stimuli and that morphine and beta-endorphin may act in different brain areas or on different receptors. 17 references. (Author abstract modified)

004179 Minchin, R. F.; Ilett, K. F.; Madsen, B. W. Dept. of Pharmacology, University of Western Australia, Nedlands, Western Australia, 6009 Australia **Effect of desmethylimipramine on tissue distribution and anorectic activity of chlorphentermine in rats.** Life Sciences. 28(17)1931-1938, 1981.

The anorectic effect and tissue distribution of chlorphentermine (CP) have been measured in the presence and absence of desmethylimipramine (DMI) in rats, following the finding that DMI is a potent displacer of CP from lung tissue in vitro. CP decreased the rate of eating without affecting onset of eating. DMI caused dose related changes in CP induced anorexia; 5mg/kg DMI inhibited the effects of CP while 7.5mg/kg DMI caused potentiation of CP. DMI significantly decreased CP concentrations in lung tissue and increased concentrations in brain, liver, and blood for up to 4 hours after treatment, but did not affect kidney or skeletal muscle levels. The CP tissue concentration time profiles for liver, brain, and kidney were significantly different in the presence and absence of DMI, suggesting nonlinear kinetics, probably due to saturable tissue binding. Using a simple model to describe eating behavior, the increased anorexia was found to be linearly related to the higher brain levels of CP seen in the presence of DMI. 23 references. (Author abstract modified)

004180 Montgomery, Tony; Willner, Paul. Willner: Dept. of Psychology, City of London Polytechnic, Old Castle Street, London E1 7NT, England **Effects of subchronic desmethylimipramine (DMI) treatment of the classically conditioned eyeblink response in rabbits.** Communications in Psychopharmacology. 4(6):519-525, 1980.

The effect of subchronic desmethylimipramine (DMI) treatment on classically conditioned eyeblink response was investigated in the rabbit. In the period following 2 weeks' treatment with this tricyclic antidepressant, rabbits were resistant to extinction of the conditioned eyeblink response. The effect was not seen during continued DMI treatment, or in animals with prior experience of extinction. Shock thresholds in DMI withdrawal did not differ from those of controls. DMI treatment did not affect initial acquisition of the response, but drugged animals did show increased responding on the first conditioning session following rest days or extinction sessions. The results extend previous observations of increased resistance to extinction of instrumental behavior in rats withdrawn from DMI. 10 references. (Author abstract modified)

004181 Morley, John E.; Levine, Allen S.; Prasad, Chandan. Neuroendocrine Research Laboratory, Minneapolis V.A. Medical Center, Minneapolis, MN 55417 **Histidyl-proline diketopiperazine decreases food intake in rats.** Brain Research. 210(1-2):475-478, 1981.

Intracerebroventricular administration of histidyl-proline diketopiperazine suppressed food intake during stress induced eating, during starvation induced eating, and over an 8 hour period of spontaneous eating in male Sprague-Dawley rats. Other cyclic piperazines failed to alter food ingestion. The suppressive effect of histidyl-proline diketopiperazine was antagonized by the enkephalin analogue D-ala-met-enkephalin. It is suggested that the two compounds may exert their mutually antagonistic effects on appetite regulation by modulation of dopamine metabolism. Histidyl-proline diketopiperazine may be the metabolically active compound responsible for the satiety observed after administration of thyrotropin releasing hormone. 19 references. (Author abstract modified)

004182 Moss, D. E.; Rogers, J. B.; Deutsch, J. A.; Salome, R. R. Dept. of Psychology, University of Texas, El Paso, TX 79968 **Time dependent changes in anterograde scopolamine-induced amnesia in rats.** Pharmacology Biochemistry and Behavior. 14(3):321-323, 1981.

Holtzman rats were trained on a Y-maze brightness discrimination task 20 minutes after i.p. injection of 2mg/kg scopolamine hydrobromide, an anticholinergic agent. Deficits in retention performance were seen 1 day and 2 weeks after training, but not at 4 or 6 weeks after training. Animals given the cholinesterase inhibitor physostigmine (0.5mg/kg) 20 minutes before retention testing also showed deficits at the first two test periods, but not at the latter two sessions. Scopolamine methyl nitrate did not induce amnesia, nor did scopolamine hydrobromide administered immediately after training. Results suggest that the presence of scopolamine in the CNS during training modifies the formation of the memory trace in such a way that memory is not available for recall for a period of weeks. 11 references. (Author abstract modified)

004183 Murphy, Michael R. Laboratory of Brain Evolution and Behavior, NIMH, Box 289, Poolesville, MD 20837 **Methadone reduces sexual performance and sexual motivation in the male Syrian golden hamster.** Pharmacology Biochemistry and Behavior. 14(4):561-567, 1981.

Methadone (1, 2, 4, 8, and 16mg/kg) caused a dose related decline in the sexual performance and sexual motivation of male Syrian golden hamsters. The debilitating effect of methadone was selective for sexual behavior, since a 16mg/kg dose completely eliminated sexual behavior without altering ambulatory activity. Naltrexone was able to prevent and reverse the effects of methadone. Results indicate that the male hamster is a good model for studies of opiate induced sexual dysfunction. These findings also support the hypothesis that endogenous opiates may be involved in the regulation of sexual behavior. 26 references. (Author abstract modified)

004184 Nagy, J. I.; Emson, P. C.; Iversen, L. L. MRC Neurochemical Pharmacology Unit, Medical Research Council Centre, Medical School, Hills Road, Cambridge, England **A reevaluation of the neurochemical and antinociceptive effects of intrathecal capsaicin in the rat.** Brain Research. 211(2):497-502, 1981.

The effects of intrathecal administration of capsaicin on thermal nociceptive threshold and on levels of substance-P, somatostatin, and glutamic acid decarboxylase in the dorsal horn of the spinal cord were studied in male Sprague-Dawley rats. Results were not consistent and suggested that intrathecal capsaicin may have induced nonspecific damage to the spinal cord. 22 references. (Author abstract modified)

004185 Nakamura, Hideo; Ishii, Katsumi; Yokoyama, Yuichi; Motoyoshi, Satoru; Natsuka, Kagayaki; Shimizu, Masanao. Shimizu: Research Laboratories, Dainippon Pharmaceutical Co., Ltd., 33-94 Enoki, 564 Suita/Osaka, Japan **Analgesic and other pharmacological activities of a new narcotic antagonist analgesic (-)-1-(3-methyl-2-butenyl)-4-(2-(3-hydroxyphenyl) 1 phenylethyl)-piperazine and its enantiomorph in experimental animals.** Journal of Pharmacy and Pharmacology. 32(9):635-642, 1980.

The stereoselectivity of 1-cyclohexyl-4-(2-(3-hydroxyphenyl)-1-phenylethyl)piperazine (I) and its 1-(3-methyl-2-butenyl) derivative (II) was demonstrated in laboratory animals. The S()-isomers of both compounds were analgesically more active than their R(-)-isomers or racemates and were 15 to 55 times as potent as morphine in ddN mice and Wistar rats. The R(-)-isomer of compound II showed analgesic potency comparable to that of pentazocine in mice, rats, and dogs and was nearly equipotent to pentazocine in reversing some actions of morphine. The amount of naloxone required to reverse the analgesic activity of the R(-)-II was about 10 times that required to antagonize the S()-isomers of compounds I and II, morphine, or pentazocine. The S()-isomers and racemates produced a Straub tail reaction and increased spontaneous locomotor activity in mice, but the R(-)-isomers did not. R(-)-II had no significant physical dependence liability in mice, rats, or rhesus monkeys and may be a useful narcotic antagonist analgesic. 57 references. (Author abstract modified)

004186 Namba, Mike M. Quock, Raymond M.; Malone, Marvin H. Physiology/Pharmacology Unit, School of Pharmacy, University of the Pacific, Stockton, CA 95211 **Effects of narcotic antagonists on L-dopa reversal of reserpine-induced catalepsy and blepharoptosis in mice.** Life Sciences. 28(14):1629-1636, 1981.

The effects of narcotic antagonists on L-DOPA reversal of reserpine induced catalepsy and blepharoptosis in mice were investigated. Reserpine induced catalepsy and blepharoptosis in mice which were readily reversed by the administration of L-DOPA. The administration of the pure narcotic antagonists naloxone and naltrexone significantly potentiated L-DOPA reversal of reserpine induced catalepsy. Lower doses of the narcotic antagonists did not significantly alter this reversal. The L-DOPA reversal of blepharoptosis was not significantly altered by either naloxone or naltrexone. These results indicate that while opiate receptors may be involved in L-DOPA reversl of catalepsy, they may not have a role in the alteration of blepharoptosis. 18 references. (Author abstract modified)

004187 Nazzaro, J. M.; Seeger, T. F.; Gardner, E. L. Gardner: Dept. of Psychiatry, Forchheimer Bldg. G54, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461 **Morphine differentially affects ventral tegmental and substantia nigra brain reward thresholds.** Pharmacology Biochemistry and Behavior. 14(3):325-331, 1981.

The effects of morphine and naloxone on intracranial self-stimulation (ICSS) were studied in male Sprague-Dawley rats with electrodes in the substantia nigra pars compacta (A-9) and the ventral tegmentum (A-10). ICSS thresholds of rats with electrodes in the A-9 nucleus were not altered by acute morphine (5.0mg/kg), but grew progressively larger with each day of morphine treatment. This threshold elevation was not reversed by naloxone given 0.5 hours after the final morphine treatment on day 5. Acute morphine significantly lowered ICSS thresholds in rats with A-10 electrodes, and tolerance to this facilitatory effect developed with chronic administration. Naloxone attenuated the lowering of ICSS threshold induced by opiate administration in animals with A-10 electrodes. Results suggest that opiates act specifically on brain systems subserving reward and reinforcement. They also suggest that the mesolimbic/mesocortical system may be involved in mediating the rewarding properties of morphine. 56 references. (Author abstract modified)

004188 Neff, N. H.; Gentleman, S.; Parenti, M.; Commissiong, J. W. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Dopaminergic neurons of spinal cord: a possible site for the action of neuroleptic drugs.** In: Usdin, E., Enzymes and neurotransmitters in mental disease. Chichester, England, John Wiley & Sons, 1980. 650 p. (p. 37-43).

The role of dopaminergic neurons in the spinal cord in normal spinal mechanisms, spinal pathology, and response to drugs is discussed. Studies in rats indicate that some of the dopaminergic neurons in spinal cord originate in the substantia nigra and enter the cord uncrossed. One of the receptors for dopamine (DA) in spinal cord may be an adenylate cyclase system similar to the cyclase system of the striatum. After transection of the spinal cord, the DA/adenylate cyclase becomes supersensitive to DA. It is suggested that the dopaminergic system of spinal cord may be implicated in the motor disturbances of Parkinson's disease and in the dyskinesia induced by treatment with neuroleptic drugs. 10 references.

004189 Nicholson, A. N.; Wright, Catherine M. Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire, England **()-6-Fluorotryptophan, an inhibitor of tryptophan hydroxylase: sleep and wakefulness in the rat.** Neuropharmacology. 20(4):335-339, 1981.

Sleep and wakefulness were studied in male Wistar rats after i.p. injection of 100mg/kg 6-fluorotryptophan (6-FT), an inhibitor of brain tryptophan hydroxylase. Wakefulness increased and REM and non-REM sleep decreased for 3 hours after injection. The time course of these effects suggested that the activity of 6-FT may be related closely to the turnover of 5-hydroxytryptamine. 17 references. (Author abstract modified)

004190 Nikoletseas, Michael M. Deree, American College of Greece, P.O. Box 18, Aghia Paraskevi, Attiki, Greece **Activity and catch-up growth in hypothyroid rats.** Pharmacology Biochemistry and Behavior. 14(4):443-446, 1981.

Wheel activity and growth were examined in hypothyroid male Sprague-Dawley rats Hypothyroidism was induced by feeding young adult rats a chow diet supplemented with propylthiouracil (PTU, 0.1% by weight) for 43 days. The wheel activity of the PTU treated rats did not differ significantly from that of euthyroid controls fed ad lib, but was significantly lower than that of pair fed controls. Bodyweight was significantly lower than that of euthyroid ad lib fed controls. Active PTU rats weighed more than pair fed active rats, but nonactive PTU rats weighed less than nonactive pair fed controls. Bodyweight and tibia length of PTU treated rats 75 days after PTU was discontinued were significantly lower than those of euthyroid rats fed ad lib, but did not differ from that of pair fed animals. It is suggested that the growth arrest observed in early hypothyroidism is partially due to factors nonspecific to thyroxine absence, such as hypophagia. 27 references. (Author abstract modified)

004191 Nomura, Yasuyuki; Segawa, Tomio. Department of Pharmacology, Inst. of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi, Hiroshima 734, Japan **Developmental change in rearing response to atropine in rats treated with 6-hydroxydopa.** Japanese Journal of Pharmacology. 30(1):109-112, 1980.

Rearing responses to atropine were studied in developing Wistar rats treated with 6-OHDOPA at birth. Atropine stimulated rearing in 23-day-old control rats, but not in 15-day-old, 18-day-old, or 20-day-old animals. Neonatal treatment with 6-OHDOPA potentiated the atropine stimulation or rearing in 23-day-old rats, but did not alter the adult response to atropine. 14 references.

004192 Ohmori, Kenji; Yamanami, Sadayoshi; Shuto, Katsuichi; Marumo, Hirofuto. Pharmaceuticals Research Laboratory, Kyowa Hakko Kogyo Co. Ltd., 1188 Nagaizumicho, Shizuoka 411, Japan **Effect of sodium dipropylacetate on conflict behavior in rats.** Japanese Journal of Pharmacology. 30(6):925-927, 1980.

The effects of sodium propylacetate (DPA), diazepam, and diphenylhydantoin on conflict behavior in male Wistar rats were compared. The drugs were administered orally, and the 3 minute conflict schedule was alternated with a variable-interval schedule (VI-2) for 12 minutes. Both 50 and 400mg/kg DPA increased the response rate suppressed by punishment, but only the 400mg/kg dose decreased the response rate in the VI-2 component. Diazepam (10 and 20mg/kg) increased the response rate in the punished component by 18% and decreased the responser rate in the VI-2 component by 50%. Diphenylhydantoin (10mg/kg) had no effect on response rate in either component. 13 references.

004193 Oka, Makoto; Yamada, Kiyoko; Yoshida, Kouichi; Shimizu, Masanao. Dept. of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co. Ltd., Suita-shi, Osaka 564, Japan **Avoidance enhancement and discriminative response control by anxiolytics with drugs acting on the GABA system.** Japanese Journal of Pharmacology. 30(3):325-336, 1980.

Experiments in male STD-ddY mice and STD-Wistar rats suggested that avoidance enhancement and discriminative response control by anxiolytic drugs may be linked to the GABA system. Chlordiazepoxide, diazepam, chlorazepate, and meprobamate increased the active avoidance rate in poorly performing mice, but chlorpromazine, haloperidol, and nortriptyline had no such effect. The effect of diazepam was potentiated by GABA and aminooxyacetic acid (AOAA); antagonized by picrotoxin and thiosemicarbazide; and not markedly influenced by spiroperidol, alpha-methyltyrosine, phenoxybenzamine, and levallorphan. The effect of other anxiolytic drugs was also potentiated by AOAA and antagonized by picrotoxin. Biperiden, methamphetamine, caffeine, and morphine also enhanced avoidance performance, but this enhancement was not altered by AOAA. In rats trained to discriminate phenobarbital from saline in a milk reinforced, two lever operant procedure, diazepam produced a dose related phenobarbital lever selection which was potentiated by AOAA and antagonized by picrotoxin. Chlordiazepoxide, chlorazepate, and meprobamate also elicited responses on the phenobarbital lever, whereas haloperidol, nortriptyline, beperiden, methamphetamine, caffeine, and morphine produced saline appropriate responding. 34 references. (Author abstract modified)

004194 Olds, M. E.; Fobes, James L.; Albert, V. Division of Biology 216-76, California Institute of Technology, Pasadena, CA 91125 **Catecholamine-serotonin interaction effects on activity in rats neonatally treated with 6-hydroxydopamine.** Psychopharmacology. 73(1):31-33, 1981.

The effect of increased central serotonergic levels on motor activity was investigated in rats neonatally treated with 6-hydroxydopamine (6-OHDA) in the lateral ventricles. Regional brain assays of monoamine levels in 90-day-old rats showed depletion of catecholamines, but not of serotonin, in the forebrain accompanied by a large elevation of norepinephrine, and minor elevation of serotonin, in the hindbrain. Measures of behavioral activity in adulthood were taken after treatment with saline, pargyline, L-tryptophan, or pargyline given 30 minutes before L-tryptophan. The combined treatment of pargyline plus L-tryptophan produced hyperactivity in controls and this effect was blocked in the 6-OHDA treated animals. These findings indicate that the serotonergic system is capable of influencing motor activity, but that this influence is blocked in animals permanently depleted of catecholamines in their terminal field regions. 19 references. (Author abstract)

004195 Ondrusek, M. Gene; Kilts, Clinton D.; Frye, Gerald D.; Mailman, Richard B.; Mueller, Robert A.; Breese, George R. Breese: Child Development Institute, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **Behavioral and biochemical studies of the scopolamine-induced reversal of neuroleptic activity.** Psychopharmacology. 73(1):17-22, 1981.

Behavioral and biochemical studies of the scopolamine induced reversal of neuroleptic activity are described. Scopolamine reversed the reduction in avoidance responding caused by spiperone and antagonized the inhibitory effects of spiperone on the behavioral actions of d-amphetamine or apomorphine. Scopolamine induced locomotor activity was greater in 6-hydroxydopamine (6-OHDA) treated animals than in controls. The possibility that presynaptic dopaminergic function was the locus of the antagonisms of spiperone by scopolamine was examined using drug interaction studies in 6-OHDA treated rats. It is concluded that scopolamine can affect both presynaptic or postsynaptic events associated with dopaminergic function and that both may contribute to the reversal of the actions of spiperone. 37 references. (Author abstract modified)

004196 Ostrowski, Nancy L.; Rowland, Neil; Foley, Teri L.; Nelson, Jeffrey L.; Reid, Larry D. Psychobiology Program, Dept. of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Morphine antagonists and consummatory behaviors.** Pharmacology Biochemistry and Behavior. 14(4):549-559, 1981.

The effects of opiate antagonists on eating and drinking were studied in male Sprague-Dawley rats. Water intake was reduced by naloxone, nalorphine, and the active isomer of WIN-44,441, but not by the inactive isomer of WIN-44,441 or by an analogue of nalorphine that does not cross the blood-brain barrier. Naloxone suppressed drinking after procedures that induce osmotic, volemic, or hormonal thirst. Naloxone suppressed eating after procedures that induce glucoprivation, but did not alter eating elicited by tail pressure. Results indicate that opiate antagonists have stereospecific effects within the CNS and suggest that endorphins play a role in the organization of ingestive behavior after challenges to homeostasis. 38 references. (Author abstract modified)

004197 Papadopoulos, Georges; Huston, Joseph P.; Nef, Barbara. Huston: Institute of Psychology III, University of Dusseldorf, Universitatsstrasse 1, D-4000 Dusseldorf, West Germany **The influence of unilateral 6-OH-dopamine lesions of the substantia nigra in the absence of the telencephalon.** Brain Research Bulletin. 6(2):165-170, 1981.

The influence of unilateral 6-hydroxydopamine (6-OHDA) lesions of the substantia nigra in the absence of the telencephalon on apomorphine and amphetamine induced turning behavior was investigated. Most detelencephalized animals exhibited spontaneous turning to the contralateral side, i.e., they no longer behaved like 6-OHDA-lesioned rats, but instead, acted like animals with nigral kainic acid or electrolytic lesions. Amphetamine increased general activity but no longer influenced turning. Apomorphine in doses of 2 to 3mg/kg completely suppressed all motility. In small doses, it reversed the spontaneous contraversive turning. This effect could be blocked by haloperidol pretreatment. High doses of haloperidol reversed the direction of circling from contraversive to ipsiversive. Arecoline induced tremor as in normal animals. Atropine did not affect turning, but increased activity level in the thalamic rats. 31 references. (Author abstract modified)

004198 Pasternak, Gavril W.; Childers, Steven R.; Snyder, Solomon H. Dept. of Neurology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 **Naloxazone, a long-acting opiate antagonist: effects on analgesia in intact animals and on opiate receptor binding in vitro.** Journal of Pharmacology and Experimental Therapeutics. 214(3):455-462, 1980.

The effects of naloxazone on analgesia in intact animals and on opiate receptor binding in vitro were investigated. Administration of naloxazone, a hydrazone derivative of naloxone, to intact mice produced a prolonged inhibition of in vitro

(3H)opiate binding lasting up to 3 days. The effect was selective since naloxazone treatment produced no changes in alpha or beta adrenergic muscarinic or benzodiazepine receptor binding, and the effects on opiate binding sites were not reproduced by nonnarcotic hydrazines. Blockade of high affinity sites by naloxazone produced an 11fold increase in the ED50 value for morphine analgesia at 24 hours with both tail flick and writhing assays. By contrast, naloxazone produced no change in the LD50 value for morphine. As high affinity binding returned to control levels over 3 days, the ED50 for morphine analgesia in naloxazone pretreated mice returned to control values. Accordingly, the analgetic, but not lethal, effects of morphine may be mediated by the high affinity subpopulation of opiate receptors. 33 references. (Author abstrct modified)

004199 Phillips, Anthony G.; McDonald, Angus C.; Wilkie, Donald M. Dept. of Psychology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Disruption of autoshaped responding to a signal of brain-stimulation reward by neuroleptic drugs.** Pharmacology Biochemistry and Behavior. 14(4):543-548, 1981.

The effects of haloperidol (0.05, 0.10, or 0.15mg/kg) and pimozide (0.15, 0.50, or 1.0mg/kg) on autoshaped responding to a signal (CS) of brain stimulation reward obtained from electrodes in the dopamine cell groups of the ventral tegmentum and adjacent substantia nigra were studied. After male Wistar rats acquired the approach to the CS, injections of pimozide or haloperidol prior to test sessions caused a significant dose related attenuation of the autoshaped approach. The drug effects did not appear to be due to direct action on sensory processes or orientation, since most of the responses after high doses of either drug occurred during the first 10 trials of 30 trial sessions. Autoshaped CS approaches declined gradually over three extinction sessions, in contrast to the rapid and sustained disruption observed during drug sessions. Results suggest that the neuroleptic induced suppression of autoshaped CS approach with brain stimulation reward cannot be attributed solely to a block of the reward process. It is suggested that neuroleptic drugs disrupt neural mechanisms by which signals of impending reward release preorganized response patterns. 38 references. (Author abstract modified)

004200 Piercey, Montford F.; Dobry, Peggy J. K.; Schroeder, Lawrence A.; Einspahr, Fred J. Upjohn Company, Kalamazoo, MI 49001 **Behavioral evidence that substance P may be a spinal cord sensory neurotransmitter.** Brain Research. 210(1-2):407-412, 1981.

Central administration of very small doses of substance-P (SP) elicited reciprocal hindlimb scratching syndromes in male CF-1 mice. SP was more potent and the onset of its effect was more rapid after intraspinal (i.s.) administration than after intracranial (i.c.) administration. After i.c. injections of radiolabeled SP, SP was recovered primarily from the brain; after i.s. injection, SP was recovered primarily from spinal cord. Correlation of the behavioral and distribution data indicated that the spinal cord is the only possible site responsible for the scratching syndrome elicited by i.s. SP. Results suggest that SP may act as a sensory neurotransmitter in the spinal cord. 39 references.

004201 Pilcher, C. W. T.; Jones, Sarah M. Dept. of Pharmacology, Faculty of Medicine, P.O. Box 24923, Kuwait, Arabian Gulf **Social crowding enhances aversiveness of naloxone in rats.** Pharmacology Biochemistry and Behavior. 14(3):299-303, 1981.

The aversiveness of naloxone was increased in male hooded rats by chronic environmental stress. All rats acquired aversions to flavored solutions that had been presented 15 minutes prior to systemic injection of naloxone, but the degree of conditioned aversion was greater in rats reared and maintained in crowded conditions. The increased aversiveness of naloxone in these rats was not attenuated by transfer from crowded conditions to individual housing 3 weeks prior to aversive conditioning. Results suggest that social interaction under conditions of chronic crowding induces a prolonged increase in the level of tonic activity in the endorphinergic system. 22 references. (Author abstract modified)

004202 Poshivalov, Vladimir P. Dept. of Pharmacology, First Pavlov Medical Institute, Leningrad, 197089, USSR **The integrity of the social hierarchy in mice following administration of psychotropic drugs.** British Journal of Pharmacology. 70(3):367-373, 1980.

Male CC57W mice in small groups developed a despotic type of social hierarchy that was resistant to the effects of psychotropic drugs. A drug induced alteration in the level of aggression in a subordinate mouse in a group of three did not alter its social position. Chronic administration of diazepam, mescaline, or droperidol altered the level of aggression and sometimes resulted in an inversion of the social hierarchy when a competitive rival was present in the group; the rate of inversion varied with the type of preexisting social hierarchy. The ability of psychotropic drugs to maintain the inertia of the hierarchy may be a useful index of the drugs' ability to alter certain types of species specific behavior, such as aggression. 15 references. (Author abstract modified)

004203 Radulovacki, Miodrag; Wojcik, Walter J.; Walovitch, Richard; Brodie, Mark. Dept. of Pharmacology, College of Medicine, University of Illinois Medical Center, 901 South Wolcott Ave., Chicago, IL 60680 **Phenoxybenzamine and bromocriptine attenuate need for REM sleep in rats.** Pharmacology Biochemistry and Behavior. 14(3):371-375, 1981.

The alpha-adrenoceptor blocker phenoxybenzamine (10mg/kg i.p.) and the dopamine receptor stimulant bromocriptine (5mg/kg i.p.) were administered to male Sprague-Dawley rats during selective REM sleep deprivation. Administration of either agent immediately before or during REM sleep deprivation prevented the appearance of REM sleep rebound. Previous studies indicated that these agents also abolish REM sleep rebound when given after REM sleep deprivation. Taken together, these findings indicate that phenoxybenzamine and bromocriptine prevent the generation of REM sleep pressure by filling the need for REM sleep. 13 references. (Author abstract modified)

004204 Raleigh, M. J.; Yuwiler, A.; Brammer, G. L.; McGuire, M. T.; Geller, E.; Flannery, J. W. Neurobiochemistry Lab. T-85, Brentwood V.A. Hospital, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073 **Peripheral correlates of serotonergically-influenced behaviors in vervet monkeys (Cercopithecus aethiops sabaeus).** Psychopharmacology. 72(3):241-246, 1981.

The relationships between 12 behaviors and three peripheral markers of central serotonergic activity were studied in vervet monkeys. Plasma free and total tryptophan correlated positively with approach, heterogrooming, and eating behaviors and correlated inversely with avoidance and solitary behaviors. The level of whole blood serotonin correlated inversely with avoidance and solitary behaviors. Results suggest that free and total tryptophan levels more accurately reflect the central serotonergic activity influencing behavior in normal vervet monkeys than does the level of whole blood serotonin. 29 references. (Author abstract modified)

004205 Reavill, C.; Jenner, P.; Leigh, N.; Marsden, C. D. University Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London, SE5, England **The role of nigral projections to the**

thalamus in drug-induced circling behaviour in the rat. Life Sciences. 28(13):1457-1466, 1981.

The role of nigral projections to the thalamus in drug induced circling behavior in the rat was investigated. Unilateral injection of 6-hydroxydopamine (6-OHDA) into the ascending nigrostriatal pathway caused contraversive circling to apomorphine and ipsiversive circling to amphetamine, respectively. An electrolesion of the ventromedial thalamic nucleus on the same side as the 6-OHDA lesion reduced apomorphine induced circling, but not that to amphetamine. Bilateral electrolesions of the ventromedial thalamic nucleus reduced neither apomorphine nor amphetamine induced circling. Electrolytic lesions of the parafascicular thalamic nucleus did not reduce apomorphine or amphetamine induced circling in animals with a unilateral 6-OHDA lesion of the nigrostriatal pathway. Knife cuts rostral and dorsal to the substantia nigra did not attenuate circling induced by injection of muscimol into the substantia nigra. Circling due to activation of nigral output pathways can be mediated by descending nigro reticular pathways. 18 references. (Author abstract modified)

004206 Reddy Ramana, S. V.; Maderdrut, Jerome L.; Yaksh, Tony L. Yaksh: Neurosurgical Research, Mayo Foundation, Rochester, MN 55901 **Spinal cord pharmacology of adrenergic agonist-mediated antinociception.** Journal of Pharmacology and Experimental Therapeutics. 213(3):525-533, 1980.

Intrathecal administration of norepinephrine (NE) and alpha-adrenergic agonists to male Sprague-Dawley rats with chronic spinal catheters elevated the nociceptive threshold in a dose dependent manner in both the hot plate and tail flick tests. Intrathecal administration of the beta-agonist isoproterenol did not alter the nociceptive threshold. The intrathecal NE effect was antagonized by pretreatment with the alpha-antagonist phentolamine, but not by the beta-antagonist propranolol. The intrathecal NE effect was not antagonized by intrathecal administration of papaverine, bradykinin, or subconvulsive doses of picrotoxin or strychinine, or by i.p. administration of naloxone or methysergide. The nociceptive threshold was significantly decreased 1 week after intrathecal administration of 6-hydroxydopamine (6-OHDA), which depleted spinal cord NE by 85%. Intrathecal tyramine elevated the nociceptive threshold but this effect was diminished in rats pretreated with 6-OHDA. The tyramine effect was antagonized by phentolamine. The intrathecal NE effect was not potentiated by aminophylline. The relative potencies of alpha-adrenergic agonists and antagonists suggested that the antinociceptive effect of intrathecal alpha-agonists is a postsynaptic receptor interaction. 81 references. (Author abstract modified)

004207 Richelle, Marc. University of Liege, Liege, Belgium **Same or different? An exploration of the behavioral effects of benzamides.** Revista Mexicana de Analisis de la Conducta. 6(2):137-155, 1980.

The behavioral effects of two benzamides (sulpiride and tiapride) were evaluated with emphasis on features that differentiate them from other drugs. Rats and cats were used, and performance was maintained by several aversive and positive reinforcement schedules. The benzamides did not simply fit into the classificatory frames of modern psychopharmacology, since several differences were evident with respect to the behavioral effects of well known compounds. The two benzamides exhibited behavioral effects on operant conditioned responses with a general trend for a depressing effect on rate of responding. Analysis of the results in various contingencies, however, did not allow classification as neuroleptics or major tranquilizers. A major difference was the contrasting resistance of learned behavior in some schedules as compared with sensitivity observed under other contingencies. 7 references. (Journal abstract modified)

004208 Ridley, R. M.; Haystead, T. A. J.; Baker, H. F. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, Middlesex, England **An analysis of visual object reversal learning in the marmoset after amphetamine and haloperidol.** Pharmacology Biochemistry and Behavior. 14(3):345-351, 1981.

The effect of amphetamine and haloperidol pretreatment on visual object reversal learning was assessed in the marmoset. Amphetamine induced perseverative responding demonstrated by high reversal learning scores and worse than chance performance in the early stages of reversal. This perseverative responding was prevented by pretreatment with haloperidol. Haloperidol, alone or in conjunction with amphetamine, caused a mild, nonperseverative impairment of reversal learning only. 24 references. (Author abstract)

004209 Ritzmann, R. F. Dept. of Physiology and Biophysics, University of Illinois Medical Center, Chicago, IL 60680 **Opiate dependence following acute injections of morphine and naloxone: the assessment of various withdrawal signs.** Pharmacology Biochemistry and Behavior. 14(4):575-577, 1981.

Injection of 100 to 150mg/kg naloxone 15 minutes after a single 50mg/kg injection of morphine induced a jumping response in male Swiss-Webster mice that was behaviorally similar to that observed during withdrawal from chronic morphine administration. The jumping response induced by acute morphine/naloxone administration was potentiated by atropine and attenuated by oxotremorine, which is consistent with the effects of these cholinergic drugs on jumping associated with morphine withdrawal. However, other symptoms associated with opiate withdrawal (hypothermia, weight loss, and diarrhea) were not produced by the acute injection of morphine and naloxone. It is suggested that this single injection paradigm is particular to the jumping response rather than a demonstration of rapid development of opiate dependence. 9 references. (Author abstract modified)

004210 Rokosz-Pelc, Anna; Antkiewicz-Michaluk, Lucyna; Vetulani, Jerzy. Vetulani: Dept. of Biochemistry, Institute of Pharmacology, Polish Academy of Sciences, 31-343 Krakow, Poland **5-Hydroxytryptamine-like properties of m-chlorophenylpiperazine: comparison with quipazine.** Journal of Pharmacy and Pharmacology. 32(3):220-222, 1980.

The effects of m-chlorophenylpiperazine (CPP) and quipazine on central serotonergic and dopaminergic function were studied in male Wistar rats. Both compounds induced the serotonin syndrome (head twitches and hind limb abduction). However, quipazine also induced locomotor stimulation and stereotyped sniffing, while CPP induced sedation. Both drugs reduced the accumulation of 5-hydroxytryptamine (5-HTP) in brain after inhibition of cerebral decarboxylase; quipazine also induced a pronounced decrease in dopa accumulation, whereas the effect of CPP on dopa appeared to be secondary to its serotonergic effect. Cyproheptadine antagonized the depression of dopa accumulation induced by CPP, but only partially antagonized the dopa depression induced by quipazine. Results suggest that CPP stimulates the central serotonergic system without directly affecting the dopamine receptor. 11 references.

004211 Rommelspacher, Hans; Nanz, Christel; Borbe, Harald O.; Fehske, Klaus J.; Muller, Walter E.; Wollert, Uwe. Muller: Pharmakologisches Institut der Universitat Mainz, D-6500 Mainz, West Germany **Benzodiazepine antagonism by harmane**

and other beta-carbolines in vitro and in vivo. European Journal of Pharmacology. 70(3):409-416, 1981.

Antagonism of benzodiazepines by harmane and other beta-carbolines was studied in female Wistar rats in vivo and in vitro. Harmane was a competitive inhibitor of benzodiazepine receptor binding in vitro and convulsions induced by harmane were reversibly inhibited by diazepam. For some beta-carboline derivatives, a correlation was found between affinity for the benzodiazepine receptor in vitro and convulsive potency in vivo. Results suggest that harmane or a related beta-carboline may be an endogenous agonist of the benzodiazepine receptor. 29 references. (Author abstract modified)

004212 Roshchina, L. F. Lab. farmakologii, Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonikidze, Moskva, USSR **/The effect of the new antidepressant inkasan on the bioelectrical activity of the brain and on conditioned reflexes./** Vliyaniye novogo antidepressanta inkazana na bioelektricheskuyu aktivnost' mozga i uslovnyye refleksy. Farmakologiya i Toksikologiya. 43(4):349-352, 1980.

The effect of the new antidepressant inkasan (3-methyl-8-methoxy-3H,1,2,5,6-tetrahydropyrazino (1,2,3-ab)-beta-carboline hydrochloride) on the bioelectrical activity of the brain and on conditioned reflexes was studied in cats, rabbits, and rats. Results show that inkasan had an activating effect on the EEG of the cerebral cortex, midbrain reticular formation, and hippocampus. Results also show that small doses of inkasan facilitated conditioned avoidance reflexes in rats, while increased doses inhibited these reflexes. 9 references. (Journal abstract modified)

004213 Russell, B.; Yaksh, T. L. Dept. of Neurological Surgery, Mayo Foundation, Rochester, MN 55901 **Antagonism by phenoxybenzamine and pentazocine of the antinociceptive effects of morphine in the spinal cord.** Neuropharmacology. 20(6):575-579, 1981.

Intrathecal administration of 0.1 to 400mcg phenoxybenzamine (PBX) or 1 to 400mcg pentazocine had no effect on hotplate or tail flick responses or on locomotor behavior in male Sprague-Dawley rats. Pretreatment with small doses of PBX (1 to 10mcg) or pentazocine (10 to 30 mcg) antagonized the antinociceptive effects of a 15mcg dose of morphine, but not those of a 3mcg dose of morphine. Larger doses of PBX or pentazocine did not alter the effect of morphine. Phentolamine (1 to 200mcg) had no effect on the antinociceptive effects of intrathecal morphine. Results suggest that pentazocine and PBX can act as partial agonists of the spinal opiate receptor. 19 references. (Author abstract modified)

004214 Schechter, Martin D. Dept. of Pharmacology, Northeastern Ohio Universities, College of Medicine, Rootstown, OH 44272 **Rapid acquisition of a two-drug discrimination: time of day effect upon saline state.** Pharmacology Biochemistry and Behavior. 14(3):269-271, 1981.

Sprague-Dawley rats were rapidly trained to discriminate between 0.8mg/kg d-amphetamine and 6mg/kg pentobarbital in a two lever food motivated operant task by imposing the drug states from the earliest stage of training (at the initiation of shaping to lever-press). Once trained, rats were given each of the training drugs and were allowed to lever-press without reinforcement until 10 responses were made on the nonpreferred lever. On this extended schedule of responding in extinction, the amphetamine induced interoceptive cue produced perseverance equal to that produced by pentobarbital. The administration of saline produced significantly more pentobarbital appropriate responding than amphetamine appropriate responding when animals were tested in the daytime, but produced random responding when animals were tested at night. Results suggest that the arousal state of the rat, a nocturnal species, may differentially influence saline tests during the day and at night. 11 references. (Author abstract modified)

004215 Schlemmer, R. Francis, Jr.; Elder, Janice K.; Casper, Regina C.; Davis, John M. Illinois State Psychiatric Institute, Dept. of Research, 1601 West Taylor St., Chicago, IL 60612 **Clonidine-induced hyperphagia in monkeys: evidence for alpha2-noradrenergic receptor mediation.** Psychopharmacology. 73(1):99-100, 1981.

The mechanism of clonidine induced hyperphagia and weight gain in monkeys was studied in 11 stumptail macaques. Clonidine induced a significant increase in food intake over baseline levels and a significant weight gain after the 3-day treatment period. Both changes induced by clonidine were antagonized by the alpha-1-noradrenergic antagonist yohimbine, but not by prazosin, an alpha-1-noradrenergic antagonist. These results suggest that clonidine induced hyperphagia and weight gain in monkeys are mediated through alpha-2-noradrenergic receptors. 11 references. (Author abstract)

004216 Schonfeld, Amy Rothman; Glick, Stanley D. Dept. of Neurology, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461 **Handling-induced seizures and rotational behavior in the Mongolian gerbil.** Pharmacology Biochemistry and Behavior. 14(4):507-516, 1981.

The relationship between sensory induced seizures, cerebral laterality (as measured by rotation), and nigrostriatal asymmetry was studied in female Mongolian gerbils. Seizure resistant gerbils made more spontaneous turns in a preferred direction than seizure sensitive animals. The antiepileptic drugs carbamazepine (10 to 20mg/kg), diazepam (16mg/kg), and pentobarbital (40mg/kg) strongly elicited rotational behavior; phenobarbital (20 to 40mg/kg) and ethosuximide (500mg/kg) potentiated rotation, but diphenylhydantoin and trimethadione were ineffective. The dopaminergic agonists amphetamine (4mg/kg) and apomorphine (16mg/kg) enhanced rotation at anticonvulsant doses, whereas the dopaminergic antagonist haloperidol reduced rotational behavior at a dose (1mg/kg) that exacerbates seizure activity. Surgical induction of nigrostriatal asymmetry had no significant effect on seizures. Results suggest that rotational behavior and seizure activity are inversely related and that the link between the two behaviors may be asymmetry in nigrostriatal dopaminergic systems. 49 references. (Author abstract modified)

004217 Severson, J. A.; Randall, P. K.; Finch, C. E. Andrus Gerontology Center, University of Southern California, Los Angeles, CA 90007 **Genotypic influences on striatal dopaminergic regulation in mice.** Brain Research. 210(1-2):201-215, 1981.

Genotypic influences on dopaminergic induced behaviors and striatal dopamine receptors were evaluated in CBA/J, C57BL/6J, and BALB/cJ male mice. Animals were tested for stereotypic responses to apomorphine, cataleptic responses to haloperidol, striatal dopamine receptor binding, dopamine levels and turnover, and responses to chronic treatment with haloperidol and bromocriptine. Results indicated that some striatal dopaminergic functions are impaired in CBA/J mice relative to the other two strains. The impaired supersensitivity responses to haloperidol in CBA/J mice were similar to those observed in aging rodents. 47 references. (Author abstract modified)

004218 Share, Norman N.; Rackham, Anita. Laboratoires Merck Sharp and Dohme-Chibret, B.P. 88, Route de Marsat, F-63203 Riom Cedex, France **Intracerebral substance P in mice: behavioral effects and narcotic agents.** Brain Research. 211(2):379-386, 1981.

A reciprocal hindlimb scratching response was induced in male Swiss mice by acute intracerebral injection of substance-P or the related undecapeptides physalaemin and eledoisin. This dose related response was not observed after injection of TRH, neurotensin, bradykinin, somatostatin, prostaglandins, dibutyryl cyclic AMP, or dibutyryl cyclic GMP. The response to intracerebral injection of substance-P was prevented by i.p. injection of analgesic narcotic agonists such as morphine in a stereospecific fashion, with a rank order of potency similar to that reported for analgesic activity and binding to opiate receptors in vitro. Narcotic agents with mixed agonist/antagonist activity were inactive. Naloxone potentiated the effect of substance-P and reversed the inhibition action of morphine. Results indicate that the reciprocal hindlimb scratching response to substance-P involves central nociceptive pathways. 26 references. (Author abstract modified)

004219 Shearman, Gary T.; Lal, Harbans. Lal: Dept. of Pharmacology, Texas College of Osteopathic Medicine, Camp Bowie at Montgomery, Fort Worth, TX 76107 **Discriminative stimulus properties of cocaine related to an anxiogenic action.** Progress in Neuro-Psychopharmacology. 5(1):57-63, 1981.

In male hooded Long-Evans rats trained to discriminate the anxiogenic action of pentylenetetrazol (20mg/kg i.p.) from saline, cocaine (20mg/kg) significantly generalized to the pentylenetetrazol discriminative stimulus. Diazepam (5mg/kg) and haloperidol (0.16 or 0.64mg/kg) did not generalize to the pentylenetetrazol cue. The discriminative stimuli produced by pentylenetetrazol and cocaine were antagonized by diazepam, but not by haloperidol. Results suggest that cocaine produces a discriminative stimulus that is related to its anxiogenic action. 27 references. (Author abstract modified)

004220 Sinclair, J. D.; Lindros, K. O. Research Laboratories, State Alcohol Monopoly (Alko), POB 350, SF-00101 Helsinki 10, Finland **Suppression of alcohol drinking with brain aldehyde dehydrogenase inhibition.** Pharmacology Biochemistry and Behavior. 14(3):377-383, 1981.

Calcium cyanamide, an aldehyde dehydrogenase (ALDH) inhibitor used in the treatment of alcoholism, suppressed voluntary consumption of ethanol by rats. Administration of a low dose of 4-methylpyrazole (4-MP) abolished acetaldehyde accumulation, but did not affect the suppression induced by cyanamide; 4-MP also failed to alter unsuppressed alcohol intake by Long-Evans rats or drinking by rats of the ANA strain developed for low levels of ethanol consumption. When given with cyanamide, 4-MP altered the development of the suppression. This effect was probably due to a decrease in the degree of brain ALDH inhibition, since a high cofrelation was found between brain ALDH activity and ethanol consumption. Results suggest that cyanamide suppresses alcohol drinking in the absence of acetaldehyde accumulation by some action related to direct inhibition of brain ALDH. 30 references. (Author abstract modified)

004221 Skolnick, Phil; Paul, Steven; Crawley, Jacqueline; Rice, Kenner; Barker, Steven; Weber, Robert; Cain, Michael; Cook, James. Laboratory of Bioorganic Chemistry, NIAMDD, NIH, Bethesda, MD 20205 **3-Hydroxymethyl-beta-carboline antagonizes some pharmacologic actions of diazepam.** European Journal of Pharmacology. 69(4):525-527, 1981.

The anxiolytic and anticonvulsant effects of diazepam in male mice were significantly reduced by 3-hydroxymethyl-beta-carboline (3-HMC) at a dose (25mg/kg) that did not alter spontaneous motor activity or elicit other overt behavioral changes. Higher doses of 3-HMC (50 to 100mg/kg) also decreased spontaneous motor activity. Results suggest that endogenous tetrahydro-beta-carbolines may interact with benzodiazepine receptors in the brain. 5 references.

004222 Smith, Donald F. Psychopharmacology Research Unit, Psychiatric Hospital, DK-8240 Risskov, Denmark **Lithium and motor activity of animals: effects and possible mechanism of action.** International Pharmacopsychiatry. 15(4):197-217, 1980.

The effects of lithium on spontaneous activity, exploratory activity, hyperactivity and stereotypy induced by drugs, drug induced hypoactivity, and activity rhythms of animals are reviewed. Attention is given to the rationale for the studies, and the relation of research on motor activity in animals to the therapeutic and prophylactic actions of lithium against manic-depressive illness. The most consistent effects of lithium on motor activity of animals are found on exploratory activity, hyperactivity, and stereotypy induced by drugs that alter monoaminergic neurotransmission, and rhythmic activity driven by endogenous biological clocks. Suppressant effects of lithium on motor activity appear related to alterations in monoaminergic and cholingeric neurotransmission to actions of thyroid hormones, and to alterations in postsynaptic depolarization. Potentiating effects of lithium on activity seem to be due to alterations in the sensitivity of monoamine receptors. Some suggestions are made concerning further studies of interest to investigate the mechanisms of action of lithium on motor activity. 129 references. (Author abstract)

004223 Smith, Donald F. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Central and peripheral effects of lithium on amphetamine-induced hyperactivity in rats.** Pharmacology Biochemistry and Behavior. 14(4):439-442, 1981.

The effects of central peripheral injections of 9.15M lithium chloride (LiCl) on open-field behavior and amphetamine induced hyperactivity in male Wistar rats were studied. Intracerebroventricular injections of LiCl (2x20mcl) did not alter open-field behavior, but antagonized amphetamine induced hyperactivity. Injection of 15ml/kg i.p. LiCl suppressed open-field activity, but did not influence the behavioral effects of amphetamine. 21 references. (Author abstract modified)

004224 Spealman, Roger D.; Katz, Jonathan L. Harvard Medical School, New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772 **Some effects of clozapine on punished responding by mice and squirrel monkeys.** Journal of Pharmacology and Experimental Therapeutics. 212(3):435-440, 1980.

The behavioral effects of clozapine, a novel antipsychotic drug, on punished responding by mice and squirrel monkeys were investigated and compared with those of chlorpromazine and chlordiazepoxide. All Ss responded under a two component fixed-ratio schedule of food presentation in which responding in one component was suppressed (punished) by delivery of electric shock after every response. Although clozapine or chlordiazepoxide increased punished responding in both species, maximal increases in punished responding produced by clozapine were less than those produced by chlordiazepoxide in squirrel monkeys. The behavioral effects of clozapine differed qualitatively from those of the antipsychotic drug, chlorpromazine, and quantitatively from those of the antianxiety drug, chlordiazepoxide. 30 references. (Author abstract modified)

004225 Spealman, Roger D.; Kelleher, R. T. New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772 **Behavioral effects of self-administered cocaine: responding maintained alternately by cocaine and electric**

shock in squirrel monkeys. Journal of Pharmacology and Experimental Therapeutics. 210(2):206-214, 1979.

Squirrel monkeys responded under a fixed-interval schedule of intravenous cocaine injection that alternated with a fixed-interval schedule of either presentation of electric shock or termination of a stimulus associated with electric shock. As the dose of cocaine was increased from 10 to 1000mcg/kg/injection, responding maintained by cocaine injection or alternatively by electric shock first increased and then decreased. The lowest doses of cocaine that reliably maintained self-administration often increased responding maintained by electric shock; the highest doses of cocaine that continued to maintain self-administration often decreased responding maintained by electric shock. When saline was substituted for cocaine, responding that had been maintained previously by cocaine injection occurred irregularly and at very low rates, whereas rates and patterns of responding maintained by electric shock were characteristic of fixed-interval schedules. When the fixed-interval schedule of cocaine injection was replaced by intravenous injections that occurred without regard to antecedent responding, the effects of cocaine on responding maintained by electric shock were found to be independent of the way in which cocaine was administered. 23 references. (Author abstract)

004226 Spirduso, Waneen W.; Abraham, Lawrence D.; Wolf, Michael D. Dept. of Physical and Health Education, University of Texas, College of Education, Austin, TX 78712 **Effects of chlorpromazine on escape and avoidance responses: a closer look.** Pharmacology Biochemistry and Behavior. 14(4):433-438, 1981.

The effects of chlorpromazine (CPZ) were evaluated in a response paradigm in which male Sprague-Dawley rats were systematically shaped over a period of days to initiate an extremely fast and consistent avoidance, consisting only of limb movements and requiring only milliseconds to complete. CPZ clearly impaired to animals' ability to initiate rapid avoidance movements. In contrast to findings in previous studies, CPZ also caused some impairment of escape responses. Results support the proposed involvement of dopamine in the initiation of voluntary movement. 23 references. (Author abstract modified)

004227 Stach, R.; Lazarova, M. B.; Kacz, D. Polish Academy of Science, Institute of Pharmacology, 12 Smetna St., 31343 Krakow, Poland **Serotonergic mechanism in seizures kindled from the rabbit amygdala.** Naunyn-Schmiedeberg's Archives of Pharmacology. 316(1):56-58, 1981.

The effects of serotonin receptor agonists and antagonists on seizures kindled from the rabbit amygdala were examined. The intensity of behavioral seizures and the duration of bioelectrical seizures were not altered by acute administration of agents that enhance serotonergic activity, including 5-hydroxytryptamine (5-HTP), quipazine, and femoxetine. Femoxetine (15mg/kg) and 5-HTP (25mg/kg) prolonged the duration of behavioral seizures. Chronic administration of 5-HTP had no effect on the development of kindled seizures. Acute administration of p-chlorophenylalanine (250mg/kg) reduced the intensity and shortened the duration of behavioral seizures, and chronic administration (80mg/kg) delayed the development of kindled seizures. Cyproheptadine shortened the duration of behavioral seizures. Results indicate that pharmacological inhibition of the serotonergic system attenuates and delays the development of seizures kindled from the amygdala, whereas pharmacological stimulation of this system has little or no enhancing effect. 18 references. (Author abstract modified)

004228 Stark, Paul; Dews, P. B. Lilly Research Laboratories, 307 E. McCarty St., Indianapolis, IN 46285 **Cannabinoids. I. Behavioral effects.** Journal of Pharmacology and Experimental Therapeutics. 214(1):124-130, 1980.

The effects of two new cannabinoids, nabilone and canbisol, were compared with those of delta9-tetrahydrocannabinol (THC) and chlordiazepoxide (CDZ) in behavioral tests in several species. The initial high activity of male Belaire Swiss mice in a photocell device was decreased by oral doses of 5 and 10mg/kg THC or 200mg/kg CDZ; 5 and 10mg/kg doses of nabilone and 2.5, 5.0, and 10.0mg/kg doses of canbisol decreased the initial high activity but increased subsequent low activity. In male Long-Evans rats, muricide and intracranial self-stimulation were slowed by THC, nabilone, and canbisol, but not by CDZ. The reactivity of rats with septal lesions was reduced by CDZ, nabilone and canbisol, but not by THC. Food consumption in rats was reduced only by nabilone and canbisol. Ataxia was induced in dogs by low i.v. doses of THC, nabilone, and canbisol; much higher doses were required when the drugs were given orally. In rhesus monkeys working under multiple fixed-ratio, fixed-interval schedules, CDZ increased responding at all doses studied, the three cannabinoids increased response rate at some doses but reduced or abolished responding at higher doses. Results indicate that nabilone and canbisol resemble CDZ in some tests and THC in others. 16 references. (Author abstract modified)

004229 Staunton, David A.; Wolfe, Barry B.; Groves, Philip M.; Molinoff, Perry B. Wolfe: Dept. of Pharmacology, University of Colorado Health Science Center, 4200 East Ninth Ave., Denver, CO 80262 **Dopamine receptor changes following destruction of the nigrostriatal pathway: lack of a relationship to rotational behavior.** Brain Research. 211(2):315-327, 1981.

The density of binding sites for (3H)spiperone in male Sprague-Dawley rat neostriatum increased gradually 2 to 3 weeks after unilateral 6-hydroxydopamine induced destruction of dopaminergic afferent neurons. The properties of the receptor labeled by (3H)spiperone were not altered by denervation. Dopamine sensitive adenylate-cyclase activity increased gradually in homogenates of the caudate ipsilateral to the lesion, compared to the contralateral side. Apomorphine induced pronounced circling in the lesioned animals, with maximal effect 3 days after the lesion. Since this effect clearly preceded receptor alterations in the striatum, the increase in the number of binding sites cannot account for the drug induced rotational behavior. 40 references. (Author abstract modified)

004230 Steinfels, George F.; Young, Gerald A. Young: Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, 636 West Lombard St., Baltimore, MD 21201 **Effects of narcotic abstinence on schedule-controlled behavior in dependent rats.** Pharmacology Biochemistry and Behavior. 14(3):393-395, 1981.

Female Sprague-Dawley rats trained to lever-press for food on a variable interval 1 minute schedule of reinforcement were made tolerant to and physically dependent on morphine or 1-alpha-acetylmethadol (LAAM). During the dependence state, behavioral tolerance was exhibited to the suppressant effect of morphine on lever-pressing, but not to the suppressant effect of LAAM. From day 4 to 12 after the morphine and LAAM injections were discontinued, mean lever-presses per session were significantly higher than predrug control values. Mean lever-presses per session were significantly higher during morphine abstinence than during LAAM abstinence. 20 references. (Author abstract modified)

004231 Sternberg, Debra B.; Gold, Paul E. Gold: Dept. of Psychology, Gilmer Hall, University of Virginia, Charlottesville, VA 22901 **Retrograde amnesia produced by electrical stimulation**

of the amygdala: attenuation with adrenergic antagonists. Brain Research. 211(1):59-65, 1981.

Subseizure electrical stimulation of the amygdala produced retrograde amnesia for a visual discrimination shock motivated task in male Sprague-Dawley rats. This amnesia was blocked by pretreatment with the alpha-adrenergic antagonist phenoxybenzamine or the beta-adrenergic antagonist propranolol. Results suggest that adrenergic mechanisms are involved in the production of retrograde amnesia. 36 references. (Author abstract modified)

004232 Stone, W. E.; Javid, M. J. Dept. of Physiology, University of Wisconsin Medical School, Madison, WI 53706 **Aminophylline and imidazole as convulsants.** Archives Internationales de Pharmacodynamie et de Therapie. 248(1):120-131, 1980.

The convulsive actions of aminophylline (APH) and imidazole (IDZ) were tested against a series of anticonvulsants in male Swiss mice. APH was significantly antagonized by phenobarbital and chlordiazepoxide, but antagonism by trimethadione was not significant. Ethosuximide, phenytoin, and aminooxyacetic acid (AOAA) potentiated APH. IDZ induced seizures were relatively refractory to anticonvulsants, but slight antagonism was seen, particularly after AOAA. Phenytoin potentiated IDZ induced seizures. Subconvulsive doses of APH and IDZ potentiated seizures induced by pentylenetetrazol and 3-mercaptopropionic acid. 35 references. (Author abstract modified)

004233 Stripling, Jeffrey S.; Hendricks, Curtis. Dept. of Psychology, University of Arkansas, Fayetteville, AR 72701 **Effect of cocaine and lidocaine on the expression of kindled seizures in the rat.** Pharmacology Biochemistry and Behavior. 14(3):397-403, 1981.

The effect of cocaine and lidocaine on the expression of kindled seizures was studied in male Long-Evans rats with electrodes implanted in the olfactory bulb, prepyriform cortex, or basolateral amygdala. Neither cocaine hydrochloride (20mg/kg i.p.) nor lidocaine hydrochloride (20mg/kg i.p.) significantly altered afterdischarge threshold. Both drugs significantly reduced the latency to clonus after stimulation, a measure presumably related to the propagation of afterdischarges from the site of stimulation to other brain areas. Both drugs also significantly reduced the behavioral response (rearing and falling) to stimulation. Cocaine significantly reduced afterdischarge duration, and lidocaine significantly reduced clonus intensity. Results indicate that cocaine has pronounced effects on the expression of seizure activity in the olfactory forebrain, some of which are due to its local anesthetic action. 39 references. (Author abstract modified)

004234 Szechtman, Henry; Hershkowitz, Moshe; Simantov, Rabi. Dept. of Neurosciences, McMaster University, Hamilton, Ontario, Canada L8S 3Z5 **Sexual behavior decreases pain sensitivity and stimulates endogenous opioids in male rats.** European Journal of Pharmacology. 70(3):279-285, 1981.

In male Wistar rats, copulation had antinociceptive effects as measured by shock induced vocalization or hindlimb withdrawal to pinch. Prolonged mating reduced the content of endogenous opioids in midbrain, but not in hypothalamus or caudate nucleus. Opiate receptor antagonism by naloxone (4mg/kg) significantly extended the postejaculatory interval. Results indicate that mating is a biological stimulus for release of endogenous opioids, possibly to prevent intense sexual stimulation from becoming aversive and to increase its reward value. 35 references. (Author abstract modified)

004235 Tang, Maisy; Ahrendsen, Kim; Falk, John L. Psychology Building, Busch Campus, Rutgers University, New Brunswick, NJ 08903 **Barbiturate dependence and drug preference.** Pharmacology Biochemistry and Behavior. 14(3):405-408, 1981.

When male Holtzman rats were exposed to a daily 3 hour session of intermittent food delivery, they orally self-administered a substantial volume (35ml) of 1mg/ml sodium phenobarbital solution during the session. These periods of voluntary phenobarbital intake had no effect on 21 hour home cage barbiturate preference. Substitution of water for phenobarbital during the session after 7.5 weeks precipitated spontaneous withdrawal signs in some animals within 24 hours of drug withdrawal, but did not alter home cage barbiturate preference. Results suggest that physical dependence alone does not play a crucial role in the maintenance of drug intake behavior. 17 references. (Author abstract modified)

004236 Teal, Janice J.; Holtzman, Stephen G. Holtzman: Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Discriminative stimulus effects of cyclazocine in the rat.** Journal of Pharmacology and Experimental Therapeutics. 212(3):368-376, 1980.

The discriminative effects of cyclazocine were investigated in two groups of rats trained to discriminate between saline and either 0.3 or 1.0 mg/kg of cyclazocine with a two choice discrete trial avoidance paradigm. Cyclazocine engendered dose related cyclazocine appropriate responding in both groups of rats with the position of the dose/response curves along the abscissa reflecting the differences in training dose. The time course of the discriminative effects of cyclazocine was relatively short; drug appropriate responding began to decline from maximal levels within 1 hour of drug administration. These and other data suggest that the discriminative effects of cyclazocine are comprised of at least two major components: 1) a narcotic component which is antagonized by naltrexone but does not appear to be mediated through the same populations of opioid receptors as morphine; and 2) a nonnarcotic component, which is not antagonized by naltrexone but mimicked by ketamine and phencyclidine. 32 references. (Author abstract modified)

004237 Threatte, Rose M.; Fregly, Melvin J.; Connor, Thomas M.; Kikta, Dianne C. Fregly: Dept. of Physiology, Box J-274, JHMHC, University of Florida, College of Medicine, Gainesville, FL 32610 **L-5-hydroxytryptophan-induced drinking in rats: possible mechanisms for induction.** Pharmacology Biochemistry and Behavior. 14(3):385-391, 1981.

The beta-adrenergic antagonist propranolol (6mg/kg i.p.) and the angiotensin converting enzyme inhibitor captopril (35mg/kg i.p.) blocked the dipsogenic responses to subcutaneous injection of L-5-hydroxytryptophan (5-HTP, 25mg/kg) in female Sprague-Dawley rats. Clonidine (12.5 and 25mcg/kg i.p.), a central alpha-adrenergic agonist that inhibits renin release, attenuated drinking 1, 2, and 3 hours after 5-HTP. Haloperidol (150mcg/kg i.p.), a dopaminergic antagonist, also attenuated the dipsogenic response to 5-HTP. Incremental reductions in 5-HTP induced drinking were observed with increasing doses of spiroperidol (37.5 to 150mcg/kg i.p.), a potent dopaminergic antagonist. Results indicate that the dipsogenic response to 5-HTP is dependent on the renin/angiotensin system and on an intact dopaminergic pathway. 25 references. (Author abstract modified)

004238 Tseng, L. -F.; Wei, E. T.; Loh, H. H.; Li, Choh Hao. Dept. of Pharmacology and Toxicology, Medical College of Wisconsin, P.O. Box 26509, Milwaukee, WI 53226 **Beta-endorphin: central sites of analgesia, catalepsy and body temperature changes in rats.** Journal of Pharmacology and Experimental Therapeutics. 214(2):328-332, 1980.

Beta-endorphin was microinjected into rat brain to localize central sites associated with some of its pharmacologic effects, namely analgesic (inhibition of tail flick response), catalepsy, and changes in body temperature. Beta-endorphin produced analgesia and catalepsy when it was injected at low doses into the medial preoptic areas, nucleus accumbens, anterior hypothalamus, and the periaqueductal gray/4th ventricular spaces. Beta-endorphin had complex effects on body temperature. For example, when it was injected into the nucleus accumbens or preoptic area, low doses produced hyperthermia; higher doses produced hypothermia. The brain regions in which low doses of beta-endorphin elicit pharmacologic effects correspond to the anatomic areas in which the endogenous beta-endorphin system is distributed. Similar correspondence to the endogenous enkephalin system was not obtained. 31 references. (Author abstract modified)

004239 Tufik, Sergio. Depto. de Psicobiologia, Escola Paulista de Medecina, Rua Botucatu, 862, 04023 Sao Paulo, Brazil **Changes of response to dopaminergic drugs in rats submitted to REM-sleep deprivation.** Psychopharmacology. 72(3):257-260, 1981.

Apomorphine, piribedil, and bromocriptine elicited aggressive behavior in male Wistar rats deprived of REM sleep. The aggressive behavior elicited by apomorphine in REM deprived animals was enhanced by treatment with haloperidol 24 hours prior to the administration of apomorphine. Haloperidol injected 2 hours prior to apomorphine treatment blocked the aggressive behavior in rats subjected to REM sleep deprivation alone or REM deprivation plus 24 hour pretreatment with haloperidol. Results support the hypothesis that the exaggerated aggressiveness elicited by apomorphine in REM deprived rats is due to postsynaptic dopaminergic receptor supersensitivity. 23 references. (Author abstract modified)

004240 Turnbull, M. J.; Wheeler, H. Wheeler: I.C.I. Pharmaceuticals Division, Bioscience Dept., Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG, England **Some observations on the pharmacological activity of MIF (Pro-Leu-Gly-NH2).** Journal of Pharmacy and Pharmacology. 32(11):803-804, 1980.

Pro-Leu-Gly-NH2 (MIF, 100mg/kg) antagonized the cataleptic effect of haloperidol (10mg/kg) in mice. However, this antagonism was observed only when MIF was injected with haloperidol or 10 minutes before or after haloperidol. The brief duration of the MIF effect may account for previous failures to observe MIF antagonism of neuroleptic induced catalepsy. 5 references.

004241 Turski, Lechoslaw; Czuczwar, Stanislaw J.; Turski, Waldemar; Kleinrok, Zdzislaw. Dept. of Pharmacology, Institute of Clinical Pathology, Medical School, Jaczewskiego 8, 20-090 Lublin, Poland **Studies of carbachol-induced wet-dog shake behavior in rats.** Psychopharmacology. 73(1):81-83, 1981.

Intraventricular administration of carbachol chloride was found to evoke wet dog shakes (WDS) in rats in a dose related manner. WDS induced by carbachol at the dose of 20mcg were antagonized by scopolamine, atropine, cyproheptadine, morphine, clonidine, phentolamine, haloperidol, and L-5-hydroxytryptophan. Methergoline, propranolol, bicuculline, and aminooxyacetic acid had no effect on carbachol induced shaking behavior. Results show the existence of different types of shaking behavior, not exclusively related to the stimulation of central serotonin structures. 23 references. (Author abstract)

004242 Valentino, Rita J.; Smith, Charles B.; Woods, James H. Dept. of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Physiological and behavioral approaches to the study of the quasi-morphine withdrawal syndrome.** Federation Proceedings. 40(5):1502-1507, 1981.

The effects of two benzazocines, UM-1037 and UM-1046, which produce a quasi morphine abstinence syndrome in normal rhesus monkeys, were characterized by the use of the isolated guinea-pig ileal preparation and by a drug discrimination procedure in pigeons. These benzazocines produce a contraction of the ileum isolated from narcotic naive guinea-pigs similar to the narcotic antagonist precipitated contraction of ilea isolated from morphine pretreated animals. This effect is suppressed by morphine, and the suppression is reversed by naloxone. The drug discrimination studies are also consistent with the involvement of cholinergic mechanisms in the behavioral effects produced by the benzazocines. The involvement of cholinergic pathways in the quasiabstinence syndrome produced by UM-1037 and UM-1046 suggests that similar pathways might be active during narcotic abstinence. 30 references. (Author abstract modified)

004243 Verberne, A. J. M.; Taylor, D. A.; Fennessy, M. R. Dept. of Pharmacology, University of Melbourne, Parkville, Victoria 3052, Australia **Attenuation of delta9-tetrahydrocannabinol-induced withdrawal-like behaviour by delta9-tetrahydrocannabinol.** Psychopharmacology. 73(1):97-98, 1981.

The effects of delta9-tetrahydrocannabinol (THC) and polyvinylpyrrolidone (PVP), the injection vehicle in which THC was suspended, on THC-induced withdrawal-like behaviour were compared. Different groups of rats were injected IV twice daily for up to 5 days with either THC, in doses increasing from 2mg/kg to 6mg/kg, or PVP. On day 6, an acute dose of 6mg/kg THC was given 30 min before IP clomipramine (15mg/kg). The total behavioral response, which included writhing, backward kicking, jumping, head shaking, and paw tremor, was attenuated in rats chronically treated with THC, but not in rats which received an acute dose of PVP. These results support the hypothesis that chronically administered THC produces a state of physical dependence in the rat. 15 references. (Author abstract modified)

004244 Verimer, Turkiz; Goodale, David B.; Long, John P.; Flynn, Jan R. Long: Dept. of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Lithium effects on haloperidol-induced pre- and postsynaptic dopamine receptor supersensitivity.** Journal of Pharmacy and Pharmacology. 32(9):665-666, 1980.

Locomotor responses to apomorphine were studied in male Sprague-Dawley rats treated chronically with haloperidol, lithium, or both. A 0.016mg/kg dose of apomorphine was required for significant inhibition of locomotor activity in rats treated chronically with lithium or saline. Doses of 0.004mg/kg and 0.008mg/kg apomorphine significantly inhibited locomotor activity in rats treated chronically with haloperidol, suggesting that chronic haloperidol induced presynaptic dopamine receptor supersensitivity. Higher doses of apomorphine increased locomotor activity, indicating activation of supersensitive postsynaptic dopamine receptors. Presynaptic and postsynaptic supersensitivities to apomorphine were not apparent in rats treated chronically with both lithium and haloperidol. Results suggest that lithium blocks the development of supersensitivity in presynaptic and postsynaptic dopamine receptors, which may account for lithium's therapeutic effects in the treatment of manic-depressive disorders and tardive dyskinesia. 6 references.

004245 Wallnau, Larry B.; Bordash, Gerard D.; Corso, Philip, Jr. Dept. of Psychology, State University College, Brockport, NY 14420 **The effects of tryptophan and manipulations of serotonergic receptors on tonic immobility in chickens.** Pharmacology Biochemistry and Behavior. 14(4):463-468, 1981.

The effects of serotonergic manipulations on tonic immobility (TI) were studied in Production Red chickens. Systemic injections of tryptophan enhanced the duration of TI. Quipazine, a serotonin (5-HT) receptor agonist, and p-chloroamphetamine, a 5-HT releaser, antagonized the effect of tryptophan and reduced the duration of TI when given alone. Fenfluramine, which promotes 5-HT release, also reduced TI duration. Pretreatment with the 5-HT receptor blocker cinanserin prevented the attenuation of TI by quipazine. Results are discussed in relation to 5-HT receptor mechanisms and the raphe model of TI. 35 references. (Author abstract modified)

004246 Wallnau, Larry B.; Bordash, Gerard D.; Corso, Philip, Jr. Dept. of Psychology, State University College, Brockport, NY 14420 **Tonic immobility in domestic fowl: possible interaction of serotonergic and dopaminergic mechanisms.** Pharmacology Biochemistry and Behavior. 14(4):469-473, 1981.

The effects of serotonin (5-HT) and dopamine (DA) receptor manipulations on tonic immobility (TI) of Production Red Chickens was examined. TI in Production Red chickens was enhanced by the DA receptor blocker haloperidol, but this effect was reversed by fenfluramine, a 5-HT receptor agonist. Tryptophan enhanced TI, but this effect was prevented by apomorphine. Results suggest that serotonergic and dopaminergic systems interact with respect to TI. 45 references. (Author abstract modified)

004247 Watanabe, Hirokazu; Nakano, Shigeyuki; Ogawa, Nobuya. Dept. of Pharmacology, Ehime University School of Medicine, Shigenobu-Cho, Onsen-Gun, Ehime-Ken, 791-02, Japan **Pharmacokinetic study of apomorphine-induced stereotypy in food deprived rats.** Pharmacology Biochemistry and Behavior. 14(4):493-496, 1981.

Apomorphine hydrochloride (10mg/kg) was administered subcutaneously to male Wistar rats with free access to food and water or deprived of food for 48 hours. Food deprivation tended to potentiate apomorphine induced stereotypy in the early stage after dosing, when plasma apomorphine concentrations were higher in food deprived rats than in ad lib controls. The potentiation of apomorphine induced stereotypy after food deprivation can be attributed in part to pharmacokinetic changes, but the exact mechanism of the effect is not yet known. 16 references. (Author abstract modified)

004248 Wei, E. T. School of Public Health, University of California, Berkeley, CA 94720 **Pharmacological aspects of shaking behavior produced by TRH, AG-3-5, and morphine withdrawal.** Federation Proceedings. 40(5):1491-1496, 1981.

Pharmacological aspects of shaking behavior produced by thyrotropin releasing hormone (TRH), AG-3-5 (1-(2-hydroxyphenyl)-4(3-nitrophenyl)-1,2,3,6-tetrahydropyrimidine-2-o ne), and morphine withdrawal are described. TRH, injected centrally at submicrogram doses, produced in nondependent, barbiturate anesthetized animals, shaking behavior identical in its general features to that of morphine withdrawal. AG-3-5, another chemical stimulant of shaking, produced specific sensations of cold in man by a peripheral site of action. Shaking movements elicited by a variety of stimuli were inhibited by central administration of nanomolar doses of drugs that act as agonists on opiate, muscarinic, and alpha-adrenergic receptors. These observations may provide information on: 1) the identity of substances in brain that, when released, provoke opiate withdrawal signs and symptoms; 2) the chemical nature of substances that stimulate peripheral cold receptors; and 3) the pharmacologic classification of centrally acting agents that attenuate withdrawal and produce antinociception. 32 references. (Author abstract modified)

004249 Weiner, William J.; Carvey, Paul; Nausieda, Paul A.; Goetz, Christopher G.; Klawans, Harold L. Dept. of Neurological Sciences, Rush-Presbyterian St. Lukes Medical Center, 1725 W. Harrison Street, Chicago, IL 60612 **The effect of chronic levodopa on haloperidol induced behavioral supersensitivity in the guinea pig.** Life Sciences. 28(19):2173-2178, 1981.

Levodopa/carbidopa was administered chronically (21 days) to male Hartley guinea-pigs made behaviorally supersensitive by prior administration of haloperidol for 21 days. Animals that showed an increased behavioral response to apomorphine after chronic haloperidol were retested for apomorphine stereotypy after levodopa/carbidopa treatment. Chronic levodopa and chronic haloperidol control groups remained supersensitive to the behavioral effect of apomorphine, but responses to apomorphine in rats treated with levodopa and haloperidol returned to normal. Results suggest that levodopa may reverse dopaminergic supersensitivity induced by neuroleptic drugs and be a useful therapeutic agent in tardive dyskinesia. 35 references. (Author abstract modified)

004250 White, Francis J.; Holohean, Alice M.; Appel, James B. Behavioral Pharmacology Laboratory, Dept. of Psychology, University of South Carolina, Columbia, SC 29208 **Lack of specificity of an animal behavior model for hallucinogenic drug action.** Pharmacology Biochemistry and Behavior. 14(3):339-343, 1981.

The frequency of limb flicking (LF) and abortive grooming (AG) was studied in cats treated with d-lysergic acid diethylamide (d-LSD), 0.01 to 0.16mg/kg) or a variety of related but nonhallucinogenic compounds. LF frequency was increased after d-LSD, lisuride, quipazine, and apomorphine. AG was increased after d-LSD, lisuride, and quipazine. Cocaine did not elicit either behavior. Results indicate that LF and AG in cats is not a reliable model of hallucinogenic drug action in humans. 43 references. (Author abstract modified)

004251 Williams, Evan F.; Rice, Kenner C.; Mattson, Mariena; Paul, Steven M.; Skolnick, Phil. Skolnick: Laboratory of Bioorganic Chemistry, NIAMDD, NIH, Building 4, Room 212, Bethesda, MD 20205 **In vivo effects of two novel alkylating benzodiazepine, irazepine and kenazepine,** Pharmacology Biochemistry and Behavior. 14(4):487-491, 1981.

Intracerebroventricular administration of the alkylating benzodiazepines irazepine or kenazepine (20nmol) resulted in complete protection against convulsant doses of pentylenetetrazole (PTZ) for at least 1 hour in NIH General Purpose mice. Significant protection against seizures was observed for at least 2 hours after irazepine and at least 4 hours after kenazepine. No anticonvulsant effects were detected after administration of the nonalkylating parent benzodiazepine Ro-7/1986 or diazepam (20 to 60nmol). Results suggest that alkylating benzodiazepines that bind to brain benzodiazepine receptors in a noncompetitive (covalent) manner in vitro can exert a long-lasting convulsant effect. 8 references. (Author abstract modified)

004252 Willner, P.; Theodorou, A.; Montgomery, A. Psychology Dept., City of London Polytechnic, Old Castle St., London E1 7NT, England **Subchronic treatment with the tricyclic antidepressant DMI increases isolation-induced fighting in rats.** Pharmacology Biochemistry and Behavior. 14(4):475-479, 1981.

Individually housed male Lister hooded rats treated with desmethylimipramine (DMI, 20mg/kg for 7 days) were more likely than controls to attack an intruder rat placed in their home cage and were more likely than controls to submit when attacked by an intruder. These behavioral changes were not seen at lower doses of DMI. Similar results were obtained when a drugged animal and control were placed together in a neutral cage; in this paradigm, lower doses of DMI were effective if the period of drug treatment was increased or if 3 to 4 days of drug withdrawal preceded behavioral testing. A dose dependent resistance to handling developed during drug treatment, and drugged animals showed weight loss and decreased open-field activity. 45 references. (Author abstract modified)

004253 Woods, J. H. Dept. of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Narcotic-reinforced responding: a rapid evaluation procedure.** Drug and Alcohol Dependence. 5:223-230, 1980.

Rhesus monkeys were conditioned to lever-press for intravenous injections of codeine. The self-injection behavior was brought under the control of a schedule of drug delivery and access to the codeine schedule was made available twice each day. Subsequently, a variety of doses of codeine and saline were compared to the dose used to condition and maintain self-injection responding. Each change in drug condition was maintained for only a single experimental session. The procedure is recommended for rapid evaluation of drugs for their capacity to reinforce self-injection behavior. (Journal abstract)

004254 Woolf, Clifford J. Dept. of Physiology, Middlesex Hospital Medical School, London W1P 6DB, England **Intrathecal high dose morphine produces hyperalgesia in the rat.** Brain Research. 209(2):491-495, 1981.

Intrathecal microinjections of high doses of morphine in the rat were found to produce algesia, hyperalgesia, and hypersthesia as opposed to the analgesia found at lower doses. This hyperalgesia is not naloxone reversible and is only partially stereospecific. Morphine-3-glucuronide produces the hyperalgesia at low doses. This morphine hyperalgesia may be mediated by a class of receptors similar to that which produces opiate induced central excitation. The intrathecal morphine hyperalgesia is of some clinical interest because of its resemblance to conditions such as trigeminal neuralgia where innocuous stimuli can provoke paroxysmal attacks of pain. 18 references. (Author abstract modified)

004255 Yakimovskiy, A. F. Lab. fiziologii vysshey nervnoy deyatel'nosti, Institut fiziologii im. I. P. Pavlova, AN SSSR, Leningrad, USSR **/Avoidance response in rats after injection of dopamine into the neostriatum./** Reaktsii izbeganiya u krys pri vvedenii dofamina v neostriatum. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova. 66(9):1312-1318, 1980.

Avoidance response after injection of dopamine into the neostriatum was studied in 39 white male rats. A conditioned avoidance reflex was developed in a chamber, half of which was dark and half of which was bright, using a metronome signal and electric shocks. Cannulas were implanted in the rostral region of the neostriatum in some of the animals and in the dorsal region in others. Tests were begun 4 to 5 days after implantation. Dopamine was administered in a physiological solution. In a control group only the solvent was administered. Results show that the avoidance response in rats is facilitated by the administration of 3mcg of dopamine in the dorsal area of the neostriatum. This suggests functional differentiation between the dorsal and ventral parts of the rat neostriatum, which probably is due to the dopaminergic nigrostriatal pathway. 20 references. (Journal abstract modified)

004256 Yamada, K.; Furukawa, T. Dept. of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **Behavior of rats and mice administered active metabolites of fluphenazine, 7-hydroxy-fluphenazine and fluphenazine-sulfoxide.** Archives Internationales de Pharmacodynamie et de Therapie. 248(1):76-85, 1980.

The behavioral effects of 7-hydroxy-fluphenazine and fluphenazine-sulfoxide, the main metabolites of fluphenazine (FZ), were studied in male ddY mice and male Wistar rats. The metabolites inhibited open-field behavior and methamphetamine induced hyperactivity, lowered body temperature, and elicited catalepsy in mice, as did FZ enanthate, FZ decanoate, and FZ dihydrochloride. After intramuscular administration, the onset of action of FZ decanoate, FZ enanthate, and their metabolites was somewhat delayed, compared to findings with FZ dihydrochloride. The duration of action of FZ enanthate and FZ decanoate was longer than that of FZ dihydrochloride and metabolites. FZ metabolites decreased stereotypy induced by 4mg/kg i.p. apomorphine and yawning elicited by 0.25mg/kg apomorphine in rats. Results suggest that 7-hydroxy-FZ and FZ-sulfoxide exert their psychotropic actions by blocking presynaptic and postsynaptic dopamine receptors and that formation of active metabolites may affect the prolonged therapeutic action of depot type preparations of FZ. 22 references. (Author abstract modified)

004257 Yanaura, Saizo; Suzuki, Tsutomu; Kawai, Teiko. Dept. of Pharmacology, Hoshi College of Pharmacy, Shinagawa-ku, Tokyo 142, Japan **Eating behavior reveals rats' preference for morphine.** Japanese Journal of Pharmacology. 30(2):145-155, 1980.

An automatic food intake measuring apparatus (food intakometer) was used to study the eating behavior of morphine dependent male Sprague-Dawley rats. Morphine dependent rats approached both morphine admixed food and drug free food at the beginning of a choice trial, but preferred the morphine admixed diet. The eating time of morphine dependent rats was prolonged compared to that of naive rats; drug dependent animals ate morphine admixed food during the day as well as at night. When dependent rats were given morphine prior to the choice trial, consumption of morphine admixed food was inhibited in a dose dependent manner and consumption of the drug free diet was increased. When dependent rats were given access to drug free food for 1 hour before the choice trial, consumption of morphine admixed food was markedly enhanced. Results suggest that rats show drug seeking behavior and are able to control their required maintenance dose. 31 references. (Author abstract modified)

004258 Yanaura, Saizo; Uesugi, Jiro; Suzuki, Tsutomu; Kawai, Teiko. Dept. of Pharmacology, Hoshi College of Pharmacy, Shinagawa-ku, Tokyo 142, Japan **Oral self-administration of morphine in rats.** Japanese Journal of Pharmacology. 30(2):258-261, 1980.

Morphine self-administration was studied in male Wistar rats in an operant discrimination task. Results indicated that rats could discriminate between morphine admixed pellets and drug free pellets and that oral ingestion of morphine reinforced lever-pressing behavior. Despite changes in the fixed-ratio schedule, the animals obtained a relatively constant dose of morphine. This finding suggests that animals may have been ingesting a maintenance level dose of morphine. 10 references.

004259 Young, Gerald A.; Wolf, Daniel L.; Steinfels, George F.; Khazan, Naim. Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, 636 West Lombard St., Baltimore, MD 21201 **Morphine challenges in levo-alpha-acetylmethadol (LAAM) post-addict rats.** Life Sciences. 28(13):1523-1527, 1981.

The EEG and behavioral effects of morphine challenges in levo-alpha-acetylmethadol (LAAM) postaddict rats were investigated. LAAM postaddict rats and control Ss were challenged with 10mg/kg of morphine at 15 days, 1 month, 3 months, and 6 months postwithdrawal. In control rats, morphine challenges produced a biphasic response consisting of 60 to 90 minutes of EEG slow-wave bursts and behavioral depression followed by 60 to 90 minutes of EEG and behavioral arousal. In LAAM postaddict rats on day 15 of abstinence, morphine challenges produced primarily EEG and behavioral arousal for 2 or 3 hours with little or no depression. At 1 and 3 months, morphine challenges still produced more immediate and sustained EEG and behavioral arousal during the initial 2 hours than in control rats. At 6 months, their responses were identical to control rats. Results are indicative of protracted abstinence in LAAM postaddict rats, and are analogous to those previously reported for morphine postaddict rats. 19 references. (Author abstract modified)

004260 Young, Richard; Glennon, Richard A.; Rosecrans, John A. Dept. of Pharmaceutical Chemistry, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Discriminative stimulus properties of the hallucinogenic agent DOM.** Communications in Psychopharmacology. 4(6):501-506, 1980.

Rats were trained to discriminate injections of the hallucinogenic agent, 2,5-dimethoxy-4-methyl-phenylisopropylamine (DOM, 1mg/kg) from saline in a two lever drug discrimination task. After the discrimination was learned, generalization of the DOM stimulus to 5-methoxy-N,N-dimethyltryptamine (5-OM DMT) was examined, as was the possible antagonism of the DOM cue response by the serotonin antagonist, pizotyline (BC-105). The results reveal that the DOM stimulus generalized to 5-OMe DMT, and that the stimulus response produced by DOM could be significantly attenuated by BC-105. It is concluded that the stimulus response of DOM and 5-OMe DMT may be mediated, at least in part, via a similar serotonergic mechanism. 7 references. (Author abstract modified)

004261 Zaikonnikova, I. V.; Val'dman, A. V.; Kozlovskaya, M. M.; Rzhevskaya, G. F. Kafedra farmakologii, Kazanskiy meditsinskiy institut im. S. V. Kurashova, Kazan', USSR **/The pharmacological characteristics of the tranquilizing effect of hydiphen./** Farmakologicheskaya kharakteristika trankviliziruyushchego deystviya gidifena. Farmakologiya i Toksikologiya. 43(4):334-338, 1980.

The pharmacological characteristics of the tranquilizing effect of hydiphen (hydrazide of diphenylphosphinylacetic acid), were studied in rats, mice, and cats. Results show that hydiphen depressed an aroused emotional state of fear and anxiety in the animals and reduced conflict in group interaction, but produced neither myorelaxation nor an increase in positive emotions. Results also show that the drug was not toxic, and had central N-cholinolytic, antiadrenergic, and antiserotoninergic effects. 13 references. (Journal abstract modified)

004262 Zimakova, I. Ye.; Kamburg, R. A.; Kirshin, S. V. Kafedra farmakologii, Kazanskiy meditsinskiy institut im. S. V. Kurashova, Kazan', USSR **/The effect of mebicar on the condition of animals under certain extreme circumstances./** Vliyaniye mebikara na sostoyaniye zhivotnykh pri nebotorykh ekstremal'nykh vozdeystviyakh. Farmakologiya i Toksikologiya. 43(4):368-371, 1980.

The effect of the new tranquilizer mebicar on the condition of rats and mice subjected to extreme stress and hypoxia was studied. Results show that: mebicar has a protective effect on some characteristics of body function under conditions of stress; the antihypoxic effect of the drug occurred with a dosage range of 100 to 1,000mg/kg, and compared favorably with the effect of sodium hydroxybutyrate; and mebicar did not affect the muscle tone, movement coordination, or working capacity of the animals. These results suggest that the normalizing effect of mebicar as a tranquilizer and antihypoxic agent may be related to its metabolic involvement. 18 references. (Journal abstract modified)

004263 Zuardi, A. W.; Finkelfarb, E.; Bueno, O. F. A.; Musty, R. E.; Karniol, I. G. Karniol: R. Jose Teodoro de Lima, 44, Bairro Cambui, CEP 13100, CAMPINAS-SP, Brazil **Characteristics of the stimulus produced by the mixture of cannabidiol with delta9-tetrahydrocannabinol.** Archives Internationales de Pharmacodynamie et de Therapie. 249(1)137-146, 1981.

Male Wistar rats trained to discriminate 5 mg/kg delta9-tetrahydrocannabinol (THC) from a control solution in a T-maze were tested for generalization to 2.5 and 1.25 mg/kg THC, 40 mg/kg cannabidol (CBD), and mixtures of 5 or 1.25mg/kg THC and 40mg/kg CBD. Doses of THC smaller than the training dose produced a progressive reduction in the number of correct responses and a decrease in running time. CBD increased running time, but did not mimic the discriminative stimulus of THC. Mixtures of CBD and THC produced THC appropriate responses only 50% of the time. Results suggest that stimultaneous administration of two cannabinoids produces a qualitative stimulus different from that produced by THC alone. 20 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

004264 Agrawal, A. K.; Seth, P. K.; Squibb, R. E.; Tilson, H. A.; Uphouse, L. L.; Bondy, Stephen C. Bondy: Laboratory of Behavioral and Neurological Toxicology, NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709 **Neurotransmitter receptors in brain regions of acrylamide-treated rats. I: Effects of a single exposure to acrylamide.** Pharmacology Biochemistry and Behavior. 14(4):527-531, 1981.

A single oral dose of 25 or 50mg/kg acrylamide increased the level of striatal 3H-spiroperidol binding in 6-week-old male Fischer rats without altering glycine, serotonin, or muscarinic cholinergic binding. A large dose (100mg/kg) of acrylamide also elevated medullary glycine and frontal cortical serotonin binding. Pretreatment with a thiol blocker or a blocker of hepatic mixed function oxidase prevented the acrylamide-induced elevation of striatal spiroperidol binding, indicating the effect of acrylamide was due to a secondary metabolite. Apomorphine-induced motility was significantly attenuated by pretreatment with acrylamide, suggesting a change in the sensitivity of the dopamine receptor. 22 references. (Author abstract modified)

004265 Bondy, S. C.; Tilson, H. A.; Agrawal, A. K. Laboratory of Behavioral and Neurological Toxicology, NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709 **Neurotransmitter receptors in brain regions of acrylamide-treated rats. II: Effects of extended exposure to acrylamide.** Pharmacology Biochemistry and Behavior. 14(4):533-537, 1981.

Administration of low doses of acrylamide (5 and 10mg/kg) to 6-week-old male Fischer rats over a 2 week period (total dose, 50 and 100mg/kg) enhanced striatal dopamine and muscarinic cholinergic receptor binding. High dose treatment (20mg/kg, given 10 times) also increased frontal cortical serotonin, medullary glycine, and cerebellar GABA receptor binding. These effects appeared to be reversible, since ligand binding in treated animals 1 week after the final acrylamide dose did not differ from control values. The increased muscarinic receptor activity appeared to be due to loss of striatal nonreceptor protein rather than increased binding, but the increased dopamine receptor binding appeared to be due to an increase in overall binding capacity. Behavioral responsiveness to apomorphine was decreased in rats treated with 10mg/kg acrylamide on 10 successive days, but this effect had dissipated within 8 days of the final acrylamide injection. 23 references. (Author abstract modified)

004266 Clanachan, A. S.; Marshall, R. J. Dept. of Pharmacology, University of Alberta, Edmonton, Alberta, Canada T6G 2H7 **Potentiation of the effects of adenosine on isolated cardiac and smooth muscle by diazepam.** British Journal of Pharmacology. 71(2):459-466, 1980.

The effects of diazepam on the negative inotropic action of adenosine in male Hartley guinea-pig atria and the adenosine mediated inhibition of neurotransmission in male Sprague-Dawley rat vas deferens were examined. Adenosine and 2-chloroadenosine produced concentration dependent inhibitions of responses of the isolated vas deferens to electrical field stimulation and concentration dependent decreases in isometric tension in the electrically driven isolated left atria. Diazepam had no direct effect on either preparation, but significantly potentiated the inhibitory action of adenosine on both tissues without altering the inhibitory effect of 2-chloroadenosine. The adenosine uptake inhibitors hydroxynitrobenzylthioguanosine (HNBTG) and dipyridamole potentiated the inhibitory action of adenosine in vas deferens, but not those of 2-chloroadenosine. Following adenosine uptake inhibition in rat vas deferens by HNBTG, diazepam failed to produce any significant additional potentiation of the inhibitory action of adenosine. It is concluded that potentiation of adenosine by diazepam may be due to inhibition of adenosine uptake. 38 references. (Author abstract modified)

004267 Gmerek, Debra E.; McCafferty, Mary R.; O'Neill, Kevin J.; Melamed, Brian R.; O'Neill, John J. O'Neill, J.: Dept. of Pharmacology, Temple University School of Medicine, 3420 N. Broad St., Philadelphia, PA 19140 **Effect of inorganic lead on rat brain mitochondrial respiration and energy production.** Journal of Neurochemistry. 36(3):1109-1113, 1981.

Toxicologically significant amounts of inorganic lead were added to male Sprague-Dawley rat brain mitochondrial preparations that did not contain ethylene-diaminetetraacetate or inorganic phosphate ions. The binding of lead to the mitochondria was measured by anodic stripping voltometry. In the presence of lead, the respiratory control ratios decreased, indicating a decrease in the degree of dependence of respiration on a phosphate acceptor. The amounts of adenosine triphosphate formed from adenosine diphosphate also decreased significantly in the presence of inorganic lead. 12 references. (Author abstract modified)

004268 Gordon, John H.; Diamond, Bruce I. Dept. of Pharmacology, University of Health Sciences/Chicago Medical School, Chicago, IL **Antagonism of dopamine supersensitivity by estrogen: neurochemical studies in an animal model of tardive dyskinesia.** Biological Psychiatry. 16(4):365-371, 1981.

Antagonism of dopamine supersensitivity by estrogen was investigated in a series of neurochemical studies in an animal model of tardive dyskinesia. The withdrawal from chronic haloperidol or estradiol benzoate (EB) treatment resulted in a behavioral supersensitivity to dopamine agonists in ovariectomized rats. On the other hand, the administration of EB during the withdrawal from haloperidol or the continuous treatment with EB attenuated or prevented the development of supersensitivity to dopamine agonists. The enhanced behavioral sensitivity to dopamine agonists was correlated with an increase in 3H-dopamine binding sites in striatal membranes. The administration of EB during the withdrawal from chronic haloperidol treatment or the continuous administration of EB decreased or prevented the proliferation of dopamine binding sites in the striatum that normally occurs upon withdrawal of these two substances. These results indicate that exogenous estrogens may modulate the number of dopamine receptors in the CNS, and, as such, may decrease the incidence and/or relieve the symptoms of tardive dyskinesia. 24 references. (Author abstract modified)

004269 Ho, C. C.; Ho, A. K. S. Laboratory of Neurochemistry and Neuropharmacology, Dept. of Basic Sciences, University of Illinois School of Medicine, Peoria, IL 61605 **Ethanol-sedative hypnotic interactions. in vitro studies on Na-K-activated adenosine triphosphatase.** Archives Internationales de Pharmacodynamie et de Therapie. 248(1):132-147, 1980.

Methaqualone and phenobarbital alone or in combination with ethanol caused a dose dependent inhibition of male Sprague-Dawley rat brain microsomal sodium and potassium activated adenosine triphosphatase (Na-K-ATPase) in vitro. The inhibitory effects were competitive with respect to K and uncompetitive with respect to magnesium (Mg) dependent ATP for phenobarbital alone or combined with ethanol. Methaqualone alone or combined with ethanol showed an uncompetitive type of inhibition with respect to Mg ATP. Dose dependent inhibition of brain Na-K-ATPase activity by disulfiram was independent of K and additive with ethanol. Pyrazole had no effect on brain Na-K-ATPase activity. Inhibition by methaqualone and phenobarbital appeared to depend on K and Na/K ratio in the reaction medium. The combined effects of ethanol and the other CNS depressants on brain Na-K-ATPase activity may contribute to their interaction toxicities. 37 references. (Author abstract modified)

004270 Imbs, Jean-Louis; Singer, Leonard; Danion, Jean-Marie; Schmidt, Mariette; Zawilslak, Richard. Institut de Pharmacologie et de Medecine experimentale, 11, rue Humann, F-67000 Strasbourg, France **Effects of indomethacin and methylprednisolone on renal elimination of lithium in the rat.** International Pharmacopsychiatry. 15(3):143-149, 1980.

The effects of human therapeutic doses of methylprednisolone and indomethacin on the urinary elimination of lithium, sodium, and phosphate in the rat were investigated. Wistar rats were given lithium chloride after treatment with indomethacin, methylprednisolone, or their solvents for 5 days. Lithium and creatinine clearance and urinary elimination of sodium and phosphate were determined. Indomethacin increased while methylprednisolone decreased the fractional tubular reabsorption of lithium. The quantity of lithium eliminated in the urine was correlated with the urinary elimination of sodium and phosphate. The effects of the anti-inflammatory drugs on renal elimination of lithium seems linked to their effects on proximal sodium reabsorption. Implications for human treatment are noted. 17 references. (Author abstract modified)

004271 Laties, Victor G.; Evans, Hugh L. Dept. of Radiation, Biology and Biophysics, University of Rochester Medical Center, Rochester, NY 14642 **Methylmercury-induced changes in operant discrimination by the pigeon.** Journal of Pharmacology and Experimental Therapeutics. 214(3):620-628, 1980.

Methylmercury-induced changes in operant discrimination by the pigeon were investigated. Pigeons were trained on a fixed consecutive number schedule of reinforcement, pecking eight or nine times on one key (a run) before making the single response on a second key that was reinforced if the number requirement had been met. Percentage of reinforcers earned and rate at which the birds pecked both decreased while variability of run length increased after enough methylmercury had been given to produce blood mercury concentrations between 13ppm and 27ppm. Some birds also showed consistent shortening of run length throughout the time of maximum poisoning. Because ataxia was a common accompaniment of the changes in operant behavior, other methods of producing ataxia were also studied in some birds. The pattern of changes induced with these methods did not match that observed after methylmercury. 26 references. (Author abstract modified)

004272 Lee, M. J.; Clement, J. G. Biomedical Section, Defence Research Establishment Suffield, Ralston, Alberta, TOJ 2NO Canada **Respiratory depression produced by diazepam in cats: effect of anaesthesia.** Archives Internationales de Pharmacodynamie et de Therapie. 248(2):289-293, 1980.

In adult cats anesthetized with chloralose, spontaneous respiration ceased within 3 minutes of injection of 0.37mg/kg diazepam into the left femoral vein. Mean arterial pressure fell from a control level of 99.4 mmHg to 32.5 mmHg. The animals recovered if artificial ventilation was initiated immediately. No respiratory depression was observed after i.v. administration of diazepam to cats anesthetized with ketamine. 12 references. (Author abstract modified)

004273 Levine, Seymour; Sowinski, Richard. Pathology Dept., New York Medical College, Westchester County Medical Center, Valhalla, NY 10595 **Lesions of amygdala, pyriform cortex and other brain structures due to dipiperidinoethane intoxication.** Journal of Neuropathology and Experimental Neurology. 39(1):56-64, 1980.

Single doses of dipiperidinoethane (DPE) produced symmetrical necrosis in pyriform cortex, amygdala, and other areas of gray matter in rats, mice, and gerbils. The necrosis was detectable in 10 hours and fully developed in 24 hours. Its distribution and severity were not influenced by carotid artery ligation. DPE was not a cumulative poison. There was a high degree of chemical specificity: neurotoxic activity was present in DPE derivatives modified by methylation of the two piperidine rings, but not in derivatives with different ring systems or different connecting chains. 18 references. (Author abstract modified)

004274 Matin, M. A.; Jaffery, F. N.; Siddiqui, R. A. Industrial Toxicology Research Centre, Post Box 80, Mahatma Gandhi Marg, Lucknow, Uttar Pradesh, India **A possible neurochemical basis of the central stimulatory effects of pp'DDT.** Journal of Neurochemistry. 36(3):1000-1005, 1981.

Oral administration of 600mg/kg 1,1,1-trichloro-2,2-bis(4'-chlorophenyl)ethane (pp'DDT) to male albino mice induced an increase in the concentration of free ammonia, a decrease in the level of GABA, and a reduction in the level of acetylcholine in the striatum. These changes were maximal 5 hours after administration, when the animals developed severe convulsions. The increase in free ammonia was not altered by drugs that abolished or reduced convulsions, such as phenobarbitone, prominal, and aminooxyacetic acid. Results suggest that pp'DDT produces stimulatory effects by increasing the concentration of ammonia, which may lower the GABA level. Changes in acetylcholine levels may be an effect of the pp'DDT-induced convulsions. 42 references. (Author abstract modified)

004275 Oktay, Sule; Onur, Rustu; Ilhan, Mustafa; Turker, R. Kazim. Turker: A. U. Tip Fakultesi, Farmakoloji Kursusu, Sihhiye, Ankara, Turkey **Potentiation of the morphine-induced respiratory rate depression by captopril.** European Journal of Pharmacology. 70(3):257-262, 1981.

Captopril, an angiotensin converting enzyme inhibitor potentiated the inhibitory effect of morphine on respiratory rate in adult albino mice. Respiratory frequency was significantly reduced by 10.0mg/kg morphine, but gradually returned to control level 2 hours after injection. No recovery was observed in the 3.5 hours after injection when 10.0mg/kg morphine was given together with captopril (0.1 and 1.0mg/kg) or after captopril pretreatment. The degree of respiratory depression in mice given 3.0mg/kg morphine after captopril pretreatment was equal to that observed after 10.0mgkg morphine alone. The possible inhibitory effect of captopril on enkephalin degrading enzymes is discussed. 20 references. (Author abstract modified)

004276 Raabe, Winfried A. Dept. of Neurology, V. A. Medical Center, Minneapolis, MN 55417 **Ammonia and disinhibition in cat motor cortex by ammonium acetate, monofluoroacetate and insulin-induced hypoglycemia.** Brain Research. 210(1-2):311-322, 1981.

Ammonia intoxication abolished the suppression of action potential generation by cortical postsynaptic inhibition by inactivating neuronal chloride ion (Cl-) extrusion in cats. The disinhibition by ammonia intoxication occurred when ammonia concentrations in cerebral cortex were increased to 320% of normal. Fluoroacetate poisoning and insulin-induced hypoglycemia also abolished suppression of action potential generation by cortical postsynaptic inhibition, but this disinhibition occurred prior to the increase in ammonia concentration associated with these conditions. Results indicate that toxic metabolic encephalopathies that increase cerebral ammonia concentrations beyond 320% of normal may produce a dysfunction in the CNS due to inactivation of neuronal Cl- extrusion, leading to ineffective cortical inhibition. However, in fluoroacetae poisoning and insulin-induced hypoglycemia, the increased ammonia concentrations in the CNS appear to have only a secondary role in initiating CNS dysfunction. 37 references. (Author abstract modified)

004277 Rebert, Charles S. Neuroscience Laboratory, SRI International, Menlo Park, CA 94025 **The brain stem auditory evoked response as a tool in neuro-behavioral toxicology and medicine.** Progress in Brain Research. 54:458-462, 1980.

Brainstem auditory evoked responses (BAERs) were recorded in Fischer rats treated daily with misonidazole. The first component of the BAER was only slightly affected, indicating little effect on the peripheral transducer or eighth nerve. Later components increased in latency, indicating a significant effect on central tract conduction velocity. Results indicate that the BAER can be a valuable tool in neurobehavioral toxicology. 15 references.

004278 Shimomura, Kyoichi; Satoh, Yoshihiko; Mori, Jo. Research Laboratories, Fujisawa Pharmaceutical Co. Ltd., Yodogawa-ku, Osaka 532, Japan **Characteristic hyperpyrexia induced by LiCl and tranylcypromine in rats.** Japanese Journal of Pharmacology. 30(2):268-271, 1980.

The monoamine oxidase inhibitor tranylcypromine (TCP, 16mg/kg) induced hyperpyrexia in male Sprague-Dawley rats pretreated with lithium chloride (250mg/kg/day for 4 days), but not in those pretreated with 250mg/kg/day sodium chloride, potassium chloride, rubidium chloride, or cesium chloride. TCP also failed to induce hyperpyrexia in rats pretreated with chlorpromazine, haloperidol, fluphenazine, sulpiride, chlordiazepoxide, diazepam, imipramine, methamphetamine, tolazoline, phentolamine, propranolol, or cyproheptadine. A low incidence of hyperpyrexia was observed in rats given pargyline, iproniazid, or nialamide after pretreatment with lithium chloride. Results indicate that hyperpyrexia is induced specifically by the combination of lithium chloride and TCP. 5 references.

004279 Stainthorp, S. F.; Morton, A. K.; Pleuvry, B. J. Pleuvry: Dept. of Pharmacology, University of Manchester, Manchester, England **The effects of nefopam on blood acid-base status in the rabbit: interactions with morphine in the mouse and rabbit.** Journal of Pharmacy and Pharmacology. 32(10):689-692, 1980.

Nefopam, a nonnarcotic analgesic with antidepressant and central muscle relaxant activity, had only minor effects on the blood pH, carbon dioxide pressure (PC02), and standard bicarbonate of conscious half lop white rabbits. However, the increase in PC02 observed after combined administration of 2.5mg/kg nefopam and 1mg/kg morphine was greater than that observed after morphine alone. Nefopam also increased the antinociceptive and respiratory depressant effects of morphine in female Manchester mice. 13 references. (Author abstract modified)

004280 Stark, Paul; Dews, P. B. Lilly Research Laboratories, 307 E. McCarty St., Indianapolis, IN 46285 **Cannabinoids. II. Cardiovascular effects.** Journal of Pharmacology and Experimental Therapeutics. 214(1):131-138, 1980.

The cardiovascular effects of two new cannabinoids, nabilone and canbisol, were compared with those of chlordiazepoxide (CDZ) and delta9-tetrahydrocannabinol (THC) in several species. In rabbits, i.v. injections of THC, nabilone, and canbisol induced modest falls in blood pressure (BP) and heartrate (HR), but CDZ had no effect. In dogs, i.v. administration of THC and CDZ had no cardiovascular effects, but nabilone caused a modest, delayed increase in BP and canbisol induced modest hypotension. Repeated daily oral administration of canbisol (0.16mg/kg) to hypertensive rats decreased BP, with no sign of tolerance to this effect. In rhesus monkeys, 0.1mg/kg THC, 0.01mg/kg nabilone, and 0.003mg/kg canbisol i.v. caused modest falls in BP with little consistent change in HR; large doses of THC, nabilone, or canbisol produced sustained hypotension interrupted by dramatic periods of hypertension. CDZ had no cardiovascular effects except in massive doses (30 and 100mg/kg), which increased BP. It is suggested that the influence of cannabinoids on behavior and skeletal muscular activity contributes to their cardiovascular effects. 10 references. (Author abstract modified)

004281 Thurston, Jean Holowach; Hauhart, Richard E.; Dirgo, John A. Dept. of Pediatrics, St. Louis Children's Hospital, 500 S. Kingshighway Blvd., P.O. Box 14871, St. Louis, MO 63178 **Effects of a single therapeutic dose of glycerol on cerebral metabolism in the brains of young mice: possible increase in brain glucose transport and glucose utilization.** Journal of Neurochemistry. 36(3):830-838, 1981.

The effects of a single dose of glycerol (2g/kg i.p.) on brain carbohydrate and energy metabolism was studied in normal nursing weanling Swiss-Webster mice. Plasma glucose increased 33% and brain glucose increased 87%, suggesting increased transport of glucose from the blood to the brain. Increases in fructose-1,6-diphosphate, lactate, alpha-ketoglutarate, and malate suggested increased metabolic flux in the glycolytic pathway and Krebs citric acid cycle. These changes may be due to the effects of the hyperosmolar glycerol solution on the blood-brain barrier and on cerebral glucose utilization. 50 references. (Author abstract modified)

004282 Waddington, John L.: Gamble, Stephen J.; Bourne, Rachel C. Division of Psychiatry, M.R.C. Clinical Research Center, Watford Road, Harrow, Middlesex HA1 3UJ, England **Sequelae of 6 months continuous administration of cis(Z)- and trans(E)-flupenthixol in the rat.** European Journal of Pharmacology. 69(4):511-513, 1981.

Male Sprague-Dawley rats were treated continuously for 6 months with cis(Z)-flupenthixol or trans(E)-flupenthixol in the drinking water. Stereotypic responses to 0.15mg/kg apomorphine were enduringly and stereospecifically antagonized by cis(Z)-flupenthixol at 0.5 to 1.0mg/kg/day or 1.4 to 3.0mg/kg/day. Responses to 1.0mg/kg apomorphine were antagonized after 5 days of cis(Z)-flupenthixol (1.4 to 3.0mg/kg/day), but were enhanced after 6 months of neuroleptic treatment. Results indicate that dopamine dependent processes may be differentially sensitive to adaptation during extended neuroleptic treatment. 10 references. (Author abstract modified)

004283 Yasuhara, Hajime; Matsuo, Hiroyuki; Sakamoto, Koji; Ueda, Issaku. Dept. of Pharmacology, School of Medicine, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142, Japan **Mechanism of membrane stabilizing and lytic effects of tricyclic antidepressants.** Japanese Journal of Pharmacology. 30(3):397-401, 1980.

The membrane stabilizing and lytic effects of tricyclic antidepressants were studied in rat erythrocytes and hepatocytes. Chlorimipramine (CIM) had a membrane stabilizing effect on erythrocytes at low concentrations and a hemolytic effect at higher concentrations, which also caused marked, temperature dependent enzyme leakage from hepatic cells. Desipramine (DMI) and imipramine (IM) also had a membrane stabilizing action on erythrocytes and hepatocytes, but these effects were not as great as those of CIM. CIM damaged the liver plasma membrane when the tissue was exposed to temperatures of 20 to 25 degrees C, whereas IM and DMI stablized the plasma membrane at this temperature range and decreased enzyme leakage from cells. Results are discussed in relation to the hepatotoxicity of tricyclic antidepressant drugs. 15 references.

004284 Zbinden, G.; Ettlin, R.; Bachmann, E. Institut fur Toxikologie, ETH, Universitat Zurich, Schorenstrasse 16, CH-8603 Zurich, Switzerland **Electrocardiographic changes in rats during chronic treatment with antidepressant and neuroleptic drugs.** Arzneimittel-Forschung. 30(10):1709-1715, 1980.

Five antidepressants, three phenothiazines and five butyrophenone neuroleptics were administered to rats orally at maximally tolerated doses for 22 weeks. The electrocardiogram (EKG) was recorded weekly. In animals treated with antidepressants, quinidine-like changes of the atrioventricular and intraventricular conduction developed. There were also elevation of T-wave, and right rotation of the electrical axis. Dibenzepine had the least effect on the EKG. In the group of phenothiazines, chlorpromazine-induced tachycardia and thioridazine widening of the QRS complex. Prothipendyl had no effect. EKG changes induced by some of the butyrophenone derivatives were tachycardia and widening of the QRS complex. In rats treated with protryptiline the EKG changes were correlated with drug concentrations in serum and myocardial tissue. The studies provide a quantitative assessment of the cardiac effects of clinically proven psychotropic drugs. They will be useful as a baseline for preclinical evaluation of new derivatives. 30 references. (Author abstract)

06 METHODS DEVELOPMENT

004285 Bohlen, Peter; Neckers, Leonard M. Neuroendocrinology Laboratories, Salk Institute, San Diego, CA 92212 **High performance liquid chromatography in the neurosciences: methodology.** In: Hanin, I., Physico-chemical methodologies in psychiatric research. New York, Raven Press, 1980. 265 p. (p. 1-22).

The methodology of high pressure liquid chromatography (HPLC) is discussed in relation to the separation and detection of substances of interest to neuroscientists. The separation processes involved in HPLC and conventional liquid chromatography are compared. Ultraviolet, fluorescence, and electrochemical detectors commonly used in HPLC are described. Although HPLC is comparable to gas chromatography/mass spectrometry (GCMS) in resolving power and detection sensitivity, it is generally better studied than GCMS for the analysis of molecules of biological origin. Separation times are usually less than 1 hour with HPLC, and sample preparation prior to chromatography is minimal. 70 references.

004286 Buu, N. T.; Duhaime, J.; Savard, C.; Truong, L.; Kuchel, O. Clinical Research Institute, 110 Pine Ave. West, Montreal, Quebec, H2W 1R7, Canada **Presence of conjugated catecholamines in rat brain: a new method of analysis of catecholamine sulfates.** Journal of Neurochemistry. 36(2):769-772, 1981.

A new method of measuring catecholamine (CA) sulfate permitted its detection in Sprague-Dawley rat brain. CA sulfate was separated from free CA by alumina adsorption followed by passage through Dowex. The CA sulfate was then measured by radioenzymatic assay in the presence of a sulfatase. Sulfate esters of dopamine, norepinephrine, and epinephrine were detected in rat hypothalamus, striatum, and hippocampus by this method. 15 references. (Author abstract modified)

004287 Carroll, Marilyn E.; Santi, Peter A.; Rudell, Richard L. Psychiatry Research Unit, Mayo Box 392, University of Minnesota, Minneapolis, MN 55455 **A microcomputer system for the control of behavioral experiments.** Pharmacology Biochemistry and Behavior. 14(3):415-417, 1981.

A self-contained microcomputer control system is described for controlling and recording events from behavioral experiments using a low cost microcomputer (the Rockwell AIM-65) and the BASIC language. Features of the system include a printer, alphanumeric display, 4K RAM, 8K BASIC on read only memory, a cassette interface, a power supply, and a control interface. The control interface allows for 16 inputs and 16 ouputs and includes a real time clock and versatile machine language subroutines for controlling and recording real time events. The use of this microcomputer system to study oral drug self-administration in rhesus monkeys is described. 5 references. (Author abstract modified)

004288 Consroe, Paul; Fish, Barbara Schneiderman. Dept. of Pharmacology and Toxicology, University of Arizona College of Pharmacy, Tucson, AZ 85721 **Behavioral pharmacology of tetrahydrocannabinol convulsions in rabbits.** Communications in Psychopharmacology. 4(4):287-291, 1980.

The behavioral pharmacology of tetrahydrocannabinol (THC) convulsion in rabbits was studied in an inbred colony of TCH seizure susceptible rabbits. THC, the major psychoactive ingredient of marihuana, causes nonfatal convulsions in a selected line of genetically unique rabbits. Convulsions occur at a minimally effective dose of .05mg/kg, and they increase in severity with increasing doses. It is noted that these THC dose findings parallel those reported for THC-induced psychoactivity in humans. These rabbit/human correlates, coupled with the specificity of rabbit response to only the psychoactive cannabinoids, add validity to the THC seizure susceptible rabbit as an animal model that is reflective of the psychoactive component of cannabinoids. 10 references. (Author abstract modified)

004289 Cowan, Alan. Dept. of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **Mini-Symposium: III. Simple in vivo tests that differentiate prototype agonists at opiate receptors.** Life Sciences. 28(14):1559-1570, 1981.

Benzomorphans that are prototype agonists at postulated opiate receptors in chronic spinal dogs have been compared using two easily quantifiable endpoints: 1) rat behavior in a Y-maze; and 2) seizure thresholds of rats exposed to flurothyl, a volatile convulsant. The sigma receptor agonists, cyclazocine and SK&F 10,047 (N-allylnormetazocine), caused naloxone insensitive behavioral arousal and bizarre behavior when rats were placed in the novel environment of a Y-maze; reverse tolerance was associated with multiple doses of cyclazocine. In contrast, phenazocine, ethylketocyclazocine and pentazocine elicited behavioral depression. In the seizure test, a consideration of qualitative effects, stereospecificity, interactions between key agonists and antagonists, and multiple dosing schedules has allowed benzomorphan agonists at mu, kappa, and sigma receptors to be grouped such that cyclazocine, phenazocine, ethylketocyclazocine and pentazocine are distinguishable from one another. It is suggested that both procedures are suitable components of a battery of standardized tests aimed at differentiating opiate receptors in vivo. 56 references. (Author abstract)

004290 Hanin, Israel; Shih, Tsung-Ming. Dept. of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Gas chromatography, mass spectrometry, and combined gas chromatography-mass spectrometry.** In: Hanin, I., Physico-chemical methodologies in psychiatric research. New York, Raven Press, 1980. 265 p. (p. 111-154).

The basic principles of gas chromatography (GC) and mass spectrometry (MS) are reviewed, and the use of combined GC/MS to separate, identify, and quantify substances of biological origin is discussed. The steps involved in setting up a GC/MS assay for qualitative or quantitative analysis are outlined. Integration of GC/MS with other laboratory techniques in studies of neurotransmitter function in the CNS is discussed. The use of GC/MS to study the incorporation of labeled dietary choline into brain acetylcholine in mice is described. 30 references.

004291 Jindal, Satya P.; Lutz, Theresa; Vestergaard, Per. Rockland Research Institute, Orangeburg, NY 10962 **GLC-mass spectrometric determination of maprotiline and its major metabolite using stable isotope-labeled analog as internal standard.** Journal of Pharmaceutical Sciences. 69(6):684-687, 1980.

A quantitative GLC/mass spectrometric assay was developed for the determination of maprotiline and its major metabolite, desmethylmaprotiline, in animal and human plasma. The assay utilizes selective ion focusing to monitor, in a GLC effluent, the fragment ions and the base peaks of maprotiline and desmethylmaprotiline trifluoroacetamides generated by electron impact ionization. Maprotiline-d3 was the internal standard. The assay can measure 2 ng of maprotiline (and the metabolite)/ml of plasma with approximately 5% precision. The curves relating the amounts of maprotiline and the metabolite added versus the amounts experimentally found over a large concentration range were linear with nearly zero intercepts and slopes of approximately 0.99 and 0.98, respectively. The method was used to study the pharmacokinetic pattern of the drug in rabbits, as well as to analyze intact maprotiline and the metabolite in patients maintained on therapeutic doses of maprotiline. Assay specificity was confirmed by complete consistency of the mass spectra of maprotiline and desmethylmaprotiline with those of the authentic materials. 22 references. (Author abstract)

004292 Kuhar, Michael J. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Autoradiographic localization of drug and neurotransmitter receptors in the brain.** Trends in NeurOSciences. 4(3):60-64, 1981.

Through the combination and adaptation of various methodologies, radiohistochemical methods for autoradiographic light microscopic localization of drug and neurotransmitter receptors in the brain can be developed. These methods are valuable complements to other histochemical methods for mapping neurotransmitters; they provide a unique view of neuroanatomy, and they can be used to provide valuable new hypotheses about how drugs produce various effects. Interesting hot spots of receptor localizations have been observed in some sensory and limbic areas of the brain. Because most available methods are light microscopic, the development of ultrastructural methods will be a necessary and important extension of this field. 20 references. (Author abstract modified)

004293 Kulmala, H. K.; Huang, C. C.; Dinerstein, R. J.; Friedman, A. M. Dept. of Pharmacological and Physiological Sciences, University of Chicago, Chicago, IL 60637 **Specific in vivo binding of 77Br-p-bromospiroperidol in rat brain: a potential tool for gamma ray imaging.** Life Sciences. 28(17):1911-1916, 1981.

The binding of the gamma labeled neuroleptic, 77Br-p-bromospiroperidol, in the rat brain was examined in vivo. This binding parrallels the binding of 3H-spiroperidol, in that binding is especially high in dopaminergically innervated areas, is saturable, and is displaced by high doses of unlabeled spiroperidol. Thus, 77Br-p-bromospiroperidol is a suitable ligand for use in gamma ray imaging techniques for in vivo monitoring of receptor binding. 22 references. (Author abstract)

004294 McCaughran, J. A.; McGeer, E. G. Dept. of Psychiatry, University of British Columbia, 2255 Westbrook Mall, Vancouver, BC, Canada V6T 1W5 **Iontophoresis of kainic acid.** Neurochemical Research. 6(1):97-98, 1981.

Iontophoresis of kainic acid (KA), using a continuous, negative 1.5mcA ejection current, from a glass pipette about 30 mcm in diameter, filled with a 10mcM solution of KA in 10mM sodium chloride, produced small, spherical lesions around the pipette tip. The area of destruction increased with time of current flow. After neostriatal injections of KA, neuronal loss (measured by the percentage decrease in choline acetyltransferase activity in whole neostriatum) was correlated with length of current flow. 1 reference.

004295 Mori, Jo; Shimomura, Kyoichi; Saitoh, Ryo; Honda, Fumio. Research Laboratories, Fujisawa Pharmaceutical Co. Ltd., 2-6-1 Kashima, Yodogawa-ku, Osaka 532, Japan **A simple histochemical screening method for amine uptake.** Japanese Journal of Pharmacology. 30(5):679-687, 1980.

A simple nonradioisotopic histochemical technique provided good semiquantitative estimates of the selectivity and potency of drug inhibitory effects on amine uptake in noradrenaline (NA), 5-hydroxytryptamine (5-HT), and dopamine (DA) containing neurons. Uptake of NA, 5-HT, and 6-HT was studied in the filum terminale of reserpinized male Sprague-Dawley rats, and DA uptake was studied in sections of the caudate nucleus. Inhibitory patterns of representative uptake inhibitors obtained by this method are consistent with those previously obtained by biochemical methods. Data from studies of imipramine, desipramine, chlorimipramine, amitriptyline, chlorpromazine, haloperidol, pimozide, sulpiride, cyproheptadine, methysergide, tryptamine, and zimelidine are presented. 31 references. (Author abstract modified)

004296 Neckers, Leonard M.; Bohlen, Peter. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **High performance liquid chromatography in the neurosciences: applications.** In: Hanin, I., Physicochemical methodologies in psychiatric research. New York, Raven Press, 1980. 265 p. (p. 23-36).

The use of high pressure liquid chromatography (HPLC) in assays of biologically relevant compounds is reviewed. The use of HPLC in the assay of serotonin, its precursors, metabolites, and relevant enzymes is described. The applicability of HPLC to analyses of amino acids, determination of drug levels in biological fluids, and monitoring of catecholamine metabolism is discussed. The use of HPLC for the assay and positive identification of biologically active peptides is also described. 50 references.

004297 Porsius, A. J. Dept. of Pharmacy, Subdivision Pharmacotherapy, University of Amsterdam, Plantage Muidergracht 24, Amsterdam, The Netherlands **The simultaneous infusion of drugs via the left and right vertebral artery of the cat; a modified animal model for the study of possible central actions of drugs upon the lower brain stem.** Archives Internationales de Pharmacodynamie et de Therapie. 248(2):260-271, 1980.

A modified animal model for the administration of drugs via the vertebral arteries (v.a.) of the cat is described. Drugs are simultaneously infused into both the left and right v.a., thereby avoiding the asymmetrical distribution pattern seen when drugs are administered to the left v.a. alone. Drug concentrations and distribution in brain are comparable to those seen after i.v. administration, but only a fraction of the i.v. dose is required. It is concluded that the modified v.a. model is an appropriate method for testing possible central actions of drugs on the pontomedullary region. 7 references. (Author abstract modified)

004298 Postmes, Th. J.; Hukkelhoven, M.; van den Bogaard, A. E. J. M.; Halders, S. G.; Coenegracht, J. Isotope Dept., St. Annadal Hospital, Maastricht, The Netherlands **Passage through the blood-brain barrier of thyrotropin-releasing hormone encapsulated in liposomes.** Journal of Pharmacy and Pharmacology. 32(10):722-724, 1980.

The effect of liposomes on the passage across the blood-brain barrier by thyrotropin releasing hormone (TRH) was studied. In mice, brain uptake of TRH was greater after i.v. injection of labeled TRH encapsulated in liposomes than after injection of free TRH. In rabbits, body temperature was significantly elevated after injection of TRH liposomes, but not after free TRH. In both species, neutral liposomes were more effective than negative liposomes. Results indicate that liposomes containing TRH can enter the brain and suggest that liposomes may be used for transport of other neuropeptides across the blood-brain barrier. 11 references.

004299 Purves, Robert D. Dept. of Anatomy and Embryology, University College London, Gower St., London WC1E 6BT, England **The physics of iontophoretic pipettes.** Journal of Neuroscience Methods. 1(2):165-178, 1979.

In a theoretical study of the release of drugs from iontophoretic pipettes, it was predicted that in the steady-state, release becomes linear with current and independent of pipette geometry when the ejecting voltage exceeds 100mV. It was also predicted that release rises slowly during an ejecting pulse to approach its steady-state value and then falls abruptly after the pulse; this asymmetry of the release curve is greatly accentuated by prior application of a retaining current. Release from pipettes of large tip diameter and cylindrical bore, such as those generally used in the CNS, should be thousands of times slower than that from pipettes of small tip diameter and large taper angle. Experimental observations of the release of an ionized fluorescent compound, quinacrine, support these predictions. 26 references. (Author abstract modified)

004300 Simon, E. J.; Bonnet, K. A.; Crain, S. M.; Groth, J.; Hiller, J. M.; Smith, J. R. New York University Medical Center, New York, NY 10016 **Recent studies on interaction between opioid peptides and their receptors.** Advances in Biochemical Psychopharmacology. 22:335-346, 1980.

Studies concerning the possible heterogeneity of opiate receptors are described, and a recently developed opiate receptor/opioid peptide culture system is discussed. These and other studies provide strong support for the existence of at least two classes of receptors, with differential affinities for opiates and enkephalins. Preliminary evidence for a heterogeneity among mu receptors is noted. It is concluded that organotypic cultures of spinal cord and attached dorsal root ganglia provide a useful model system for the analysis of cellular mechanisms underlying both acute and chronic effects of opiates and of the functional significance of the opiate receptor/enkephalin system. 25 references.

004301 Tadano, Takeshi; Endo, Yasuo; Kisara, Kensuke. Dept. of Pharmacology, Tohoku College of Pharmacy, Sendai 983, Japan **A simple determination of serotonin, 5-hydroxyindoleacetic acid and 5-hydroxytryptophan decarboxylase activity in rat brain areas and parallel correlation among the levels.** Japanese Journal of Pharmacology. 30(3):347-356, 1980.

Small P-cellulose and DEAE-Sephadex columns were used to separate serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA). Both substances were estimated fluormetrically by the reaction with o-phthalaldehyde. Recoveries of 5-HT and 5-HIAA were 80 and 71%, respectively. The complete separation of 5-hydroxytryptophan (5-HTP) from 5-HT made it possible to determine 5-HTP decarboxylase activity in male Wistar rat brain regions without using an isotope labeled substrate. Enzyme activities in discrete areas paralleled 5-HT levels, except in the striatum, where enzyme activity was markedly elevated. Levels of 5-HIAA also paralleled those of 5-HT. 32 references. (Author abstract modified)

004302 Takahashi, David M. Food and Drug Administration, 50 United Nations Plaza, San Francisco, CA 94102 **Rapid determination of chlorpromazine hydrochloride and two oxidation products in various pharmaceutical samples using high-performance liquid chromatography and fluorescence detection.** Journal of Pharmaceutical Sciences. 69(2):184-187, 1980.

A rapid, simple, and accurate high performance liquid chromatographic procedure using an amino bonded microparticulate column was developed for the determination of chlorpromazine hydrochloride and its two sulfoxide and sulfone oxidation products in commercially available pharmaceutical dosage preparations. Simultaneous identification and quantitation of the oxidation products in the presence of at least 100 times the amount of parent compound were achieved with selective fluorometric detection. Identification and quantitation of the parent compound were achieved by changing the fluorescence detection mode. A typical chromatographic run was complete within 15 minutes, and quantitation of the oxidation products at levels as low as 0.1mcg (0.1% contamination) was demonstrated. 13 references. (Author abstract modified)

004303 Warsh, Jerry J.; Godse, Damodar D.; Cheung, Siu W.; Li, Peter P. Sec. of Biochemical Psychiatry, Clarke Institute of Psychiatry, University of Toronto, 250 College St., Toronto, Ontario M5T 1R8, Canada **Rat brain and plasma norepinephrine glycol metabolites determined by gas chromatography-mass fragmentography.** Journal of Neurochemistry. 36(3):893-901, 1981.

A gas chromatographic/mass fragmentographic procedure was used for simultaneous quantitation of 3,4-dihydroxyphenylethyleneglycol (DHPG) and 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) in male Wistar rat and male Swiss-Webster mouse brain and plasma. Whole rat brain total and free DHPG concentrations were similar to total and free MHPG levels. Total DHPG concentrations exceeded total MHPG concentration in hypothalamus, midbrain, pons/medulla, and hippocampus. In other brain regions, levels of these metabolites were similar. In plasma, total DHPG levels were only 20% as high as MHPG levels. In mouse brain, DHPG and MHPG occurred almost entirely in free form. Total DHPG levels were only 50% as high as MHPG concentrations. Results suggest that DHPG formation and efflux may be more important than MHPG in the metabolic clearance of CNS norepinephrine in some species. 30 references. (Author abstract modified)

004304 Weeks, James R. Experimental Biology, Upjohn Company, Kalamazoo, MI 49001 **An improved pneumatic syringe for self-administration of drugs by rats.** Pharmacology Biochemistry and Behavior. 14(4):573-574, 1981.

An improved pneumatic syringe for self-administration of drugs by rats is described. A pneumatic cylinder operates the plunger of the microliter syringe and a three way valve switches the syringe between a solution reservoir and the animal. An electrically operated subminiature solenoid valve has been substituted for the mechanical valve previously used. The new design eliminates several components, making the device more compact and easier to use. 3 references. (Author abstract modified)

004305 Westerink, B. H. C.; Mulder, T. B. A. Pharmaceutical Lab., University of Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands **Determination of picomole amounts of dopamine, noradrenaline, 3,4-dihydroxyphenylalanine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, and 5-hydroxyindolacetic acid in nervous tissue after one-step purification on Sephadex G-10, using high.** Journal of Neurochemistry. 36(4):1449-1462, 1981.

A procedure for the determination of dopamine (DA), noradrenaline (NA), 3,4-dihydroxyphenylalanine (DOPA), 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), and 5-hydroxyindolacetic acid (5-HIAA) in nervous tissue after one step purification on Sephadex G-10, using high performance liquid chromatography with a novel type of electrochemical detection, is described. The method is based on a rapidly performed isolation of DA, NA, DOPA, DOPAC, HVA, and 5-HIAA from one nervous tissue sample on small columns of Sephadex G-10, followed by reverse phase high performance liquid chromatography with electrochemical detection. A new type of electrochemical detector based on a rotating disk electrode (RDE) was used. The RDE was found to be a reliable and sensitive amperometric detector with several advantages over the currently used thin layer cells. Endogenous concentrations of DA, NA, DOPA, DOPAC, HVA, and 5-HIAA in eight rat brain regions is described. 26 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

004306 Boyd, E. J. S.; Wormsley, K. G. Wormsley: Ninewells Hospital, Ninewells, Dundee DD1 9SY, Scotland **Inhibition of pentagastrin-stimulated and overnight gastric secretion by LM24056, a new phenothiazine-derived antisecretory drug.** Lancet. No. 8218:471-473, 1981.

The inhibition of pentagastrin stimulated and overnight gastric secretion by LM24056, a new phenothiazine derived antisecretory drug, is described. LM24056, a tricyclic drug, weakly inhibited pentagastrin stimulated gastric secretion but was a powerful inhibitor of nocturnal gastric secretion in five healthy volunteers. In 23 patients with duodenal ulcer, LM24056 at doses of 100mg, 200mg, and 300mg inhibited overnight acid output by 31%, 70%, and 81%, and overnight pepsin secretion by 15%, 50%, and 69%, respectively. In view of its gastric inhibitory effects, LM24056 warrants clinical evaluation in the treatment of peptic ulcer disease. 2 references. (Author abstract modified)

004307 Cassagnes, J.; Lamaison, D.; Palcoux, M. C.; Lusson, J. R.; Fanget, M.; Gachy, B.; Teyssoneyre, B.; Jallut, H. C.H.R. De Clermont-Fd, B.P. 69, F-63003 Clermont-Ferrand Cedex, France **/Treatment of unstable angina by diltiazem./** Traitement du syndrome de menace par le diltiazem. Therapie. 35(4):465-473, 1980.

The antianginal effect of diltiazem, a new calcium antagonist, was studied. Eighty seven patients, 24 with variant angina and 63 with common instable angina in which beta-blocking agents and/or amiodarone and/or perhixilline had failed to suppress symptoms of recurrent angina pectoris at rest, were given 180mg/day of diltiazem (later increased in some cases to as much as 360mg/day). Ss were followed for an average of 8 months. Results show persistent improvement in 78% of patients with variant and 65% of patients with common instable angina. Adverse side-effects were low. 28 references. (Journal abstract modified)

004308 Diricq, St.; Ansseau, M. Universite de Liege, Clinique Medico-Psychologique, Place du 20-Aout 7, Liege, Belgium. **/ Therapeutic news./** Actualites therapeutiques. Feuillets Psychiatriques de Liege. 12(1-2):1-26, 1979.

Several new psychotropic drugs are evaluated. The registered name, producing laboratory, international chemical denomination, formula, chemical class, usual dosage, principle indications, counterindications, and usual adverse side-effects are listed for each drug. The drugs evaluated include: the hypnotics flunitrazepam and triazolam; the psychorelaxants temazepam, camazepam, and clorazepate dipotassium; the neuroleptics melperone, pipotiazine, clopenthixol decanoate, tiapride, sultopride, and loxapine succinate; the antidepressants butriptyline, maprotiline, viloxazine, and mianserin; and pizotifen and Neurolithium. 9 references.

004309 Jovanovic, U. J.; Ott, H.; Heidrich, H.; Stephan, K.; Schratzer, M. University of Wurzburg, Psychiatric Clinic, Wurzburg, West Germany **Age-specific doses of lormetazepam as a night sedative in cases of chronic sleep disturbance.** Waking and Sleeping. 4(3):223-235, 1980.

Various doses of lormetazepam, a benzodiaze pinederivative, were examined to determine the optimal dosage for different age groups of outpatients with chronic sleep disturbance. Ss were 120 patients who were divided into a younger group (aged 20 to 55 years) and an older group (aged 56 to 85 years). Four different doses were given to each age group. A preplacebo week preceded the experiment 2 weeks, which were followed by a postplacebo week. No differences in effects between the different doses were observed with regard to sleep pattern variables (sleep latency, sleep duration, frequency of awakenings, sleep quality, and occurrence of bad dreams), with the exception of sleep quality which was better in the older group than in the younger group after 0.5mg. Considerable differences with regard to hangover feelings the next morning and small differences in side-effects were found. Findings indicate the 0.5mg dose is superior for the older group and the 1.0mg dose is recommended for the younger age group due to fewer side-effects. 12 references. (Author abstract modified)

004310 Shulgin, Alexander T.; Carter, Michael F. 1483 Shulgin Road, Lafayette, CA 94549 **N,N-diisopropyltryptamine (DIPT) and 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT). Two orally active tryptamine analogs with CNS activity.** Communications in Psychopharmacology. 4(5):363-369, 1980.

The synthesis and preliminary human psychopharmacology of two tryptamine analogs, N,N-diisopropyltryptamine (DIPT) and 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT), in which the basic amine function is sterically hindered is reported. Although these analogs are active in man only parenterally, it has been found that the N-isopropyl homologs of these two bases are both orally active and have human potency similar to their methyl counterparts. DIPT effects a passive and neutral psychotomimetic state, but one that embodies an unusual degree of auditory distortion, both in the pitch and the timbre of perceived sounds. 5-MeO-DIPT, on the other hand, produces a talkative and disinhibited state with easy emotional expression. 14 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

004311 Alfredsson, Gunnel; Sedvall, Goran. Laboratory of Experimental Psychiatry, Dept. of Psychiatry, Karolinska Hospital, Karolinska Institute, S-104 07 Stockholm, Sweden **Protein binding of chlorpromazine in cerebrospinal fluid and serum.** International Pharmacopsychiatry. 15(5):261-269, 1980.

The binding of chlorpromazine to protein in human cerebrospinal fluid (CSF) was measured by equilibrium dialysis. In CSF from schizophrenic patients binding of chlorpromazine was found to vary by between 19 and 72%. There was no correlation between the degree of binding and the total amount of protein in the CSF. When chlorpromazine was equilibrated between CSF and serum in vitro almost the same distribution was found as obtained in vivo in drug treated patients. It is concluded that there is rapid equilibrium between chlorpromazine in body fluids in vivo, and that active transport of chlorpromazine between these body fluids is negligible. 12 references. (Author abstract modified)

004312 Beramendi, V.; Alpert, M.; Guimon, J.; Friedhoff, A.; Gutierrez, M. Facultad de Medicine, Universidad de Bilbao, Bilbao, Spain **/A controlled study of L-dopa in schizophrenia with reference to the theory of dopaminergic receptor hypersensitivity./** Estudio controlado de la L-dopa en la esquizofrenia con referencia a la teoria de la hipersensibilidad de los receptores dopaminergicos. Archivos de Neurobiologia. 63(2):107-124, 1980.

In a controlled study of the dopaminergic receptor hypersensitivity hypothesis in schizophrenia, 31 schizophrenic patients were assigned to one of three treatment groups: 12 received levodopa-carbidopa (maximum dosage 1500mg/day); 9 received haloperidol (maximum 20mg/day); and 10 received placebo. The group receiving L-dopa-carbidopa went through the 3 phases: 1) deterioration for 45 days; 2) adaptation for a month; and 3) improvement for 45 days in (5 of 10 clinical cases). Greatest improvement was found for the haloperidol group. Results suggest that deterioration of the clinical state after several weeks of high dosage L-dopa-carbidopa was less than would be predicted by the dopaminergic hypersensitivity hypothesis. Initial clinical deterioration produced by L-dopa appears to be owing more to a diffuse psychotoxic effect than to worsening of the schizophrenic symptomatology. 29 references. (Author abstract modified)

004313 Berger, Philip A. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Endorphins in psychopathology.** Research Report, NIMH Grant MH-30854, 1980. 20 p.

Research on the possible connections between endorphins and schizophrenia is reported which utilized three strategies: 1) measurement of the concentration of endorphins in biological fluids and spinal fluid of patients and control Ss; 2) administration of endorphin as an experimental treatment for schizophrenia; and 3) administration of the opiate and endorphin antagonist, naloxone. The data obtained from these studies is seen as indicating the tenuous and inconsistent connection between endorphins and schizophrenia. Patients did not seem to have elevated concentrations of beta-endorphin (beta-END) in spinal fluid, plasma, or dialysate. In 16 placebo controlled double-blind trials in chronic schizophrenics, high doses of intravenous naloxone produced significant decreases in hallucinations. beta-END injected intravenously also had pharmacological activity. Possible explanations for the contradictory findings are offered, ranging from basic biochemical to clinical hypotheses. The need for further research using the pure opiate antagonist, naloxone, is discussed. 56 references.

004314 Berger, Philip A.; Barchas, Jack D. Stanford University School of Medicine, Stanford, CA 94305 **Drugs and schizophrenia.** In: Melmon, K., Drug therapeutics: concepts for physicians. New York, Elsevier/North Holland, 1980. (p. 35-64).

The pharmacotherapy of schizophrenia and the biochemical hypotheses these treatments have generated are reviewed, as are the history of schizophrenia and the history of neuroleptics. The clinical syndrome of schizophrenia is delineated as is the efficacy of neuroleptic medication in its treatment. Neuroleptics have helped psychiatrists to become quantitative in the diagnosis and treatment of schizophrenia and have helped link psychiatry with the biological sciences. The dopamine hypothesis of neuroleptic drug action offers hope for the understanding of the biochemical basis of schizophrenia. Acetylcholine, GABA, and the endorphines may all play a role in schizophrenia, and future research may implicate neuroregulators not yet discovered. While the neuroleptics ameliorate schizophrenic symptoms they do not cure, and the patient may develop tardive dyskinesia or other side-effects. Thus, a better understanding of the multiple biochemical contributors to schizophrenia is needed and could facilitate the development of pharmacologic treatments for the disorder based on altering neurotransmitters other than dopamine or based on physiological mechanisms that do not involve chemical neurotransmitters. 68 references.

004315 Brosteanu, E. R.; Floru, L. University Psychiatric Clinic, Rhineland Regional Hospital, Dusseldorf, West Germany **Correlations between visual evoked potentials and psychopathological findings in schizophrenic patients under treatment with various psychopharmacological drugs.** In: Barber, C., Evoked potentials. Baltimore, MD, University Park Press, 1980. 614 p. (p. 549-556).

Two questions with regard to the study of the psychopathology of schizophrenic patients by the use of evoked potentials (EPs) were examined: 1) do certain symptoms or syndromes find expression in the EP findings at all and, if so, can there be a definite line drawn between such findings on the one hand and any individual deviations or the effect of psychopharmacological drugs and their side-effects on the other; and 2) is there a possibility of establishing, by means of the EP, a statistically validated predictability with regard to clinical responsiveness, particularly regarding clinical changes. Solely by analyzing the ratio of time or rather the shifting of the components, latency intervals, it was possible to establish that improvements or deteriorations of the different cardinal symptoms of the schizophrenic syndrome are in fact reflected in the course of the visual evoked potential findings. It is suggested that a simple and appropriate method of predicting relapses and their timely treatment can be developed from an analysis of slopes and principal factors of the EP latencies and the functional component groups. 6 references.

004316 Davis, Glenn C.; Buchsbaum, Monte S.; Bunney, William E., Jr. Dept. of Psychiatry, University of Tennessee School of Medicine, Memphis, TN 38104 **Alterations of evoked potentials link research in attention dysfunction to peptide response symptoms of schizophrenia.** Advances in Biochemical Psychopharmacology. 22:473-487, 1980.

Current research in the psychophysiology of attention dysfunction in schizophrenia and research studies proposing a pathological role for endorphins in schizophrenia are reviewed. Evoked potential studies are described which support the endorphin hypothesis of schizophrenia and link attention dysfunction to abnormal pain perception. Changes in the amplitude of a specific evoked potential component, the N120, form the basis of this linkage. Reduced N120 amplitudes in the visual and somatosensory modalities in schizophrenic Ss, the reversal of this with chronic naltrexone, and its simulation with morphine in normal volunteers are reported. 53 references. (Author abstract modified)

004317 Davis, Glenn C; Bunney, William E., Jr. Dept. of Psychiatry, University of Tennessee Center for Study of Health Sciences, Memphis, TN 38104 **Psychopathology and endorphins.** Advances in Biochemical Psychopharmacology. 22:455-463, 1980.

The roles of endorphins in psychiatric illness (particularly schizophrenia and depression) are reviewed. It is noted that suggestive evidence exists linking endorphins to the schizophrenic syndrome. Narcotic antagonists appear to slightly attenuate some symptoms; attentional performance is improved, and cerebrospinal fluid (CSF) opiate binding substances are reported elevated in a subgroup of patients. Fewer affectively ill patients have been studied, and little evidence has accumulated suggesting a relationship between symptoms of affective illness and endorphins. However, CSF endorphins appear elevated in some manic-depressive patients, and pain patients with depression have higher CSF endorphins than pain patients without depression. 42 references. (Author abstract modified)

004318 Dotti, Andreai Lostia, Onofrio; Rubino, Ivo A.; Bersani, Giuseppe; Carilli, Luciana; Zorretta, Domenico. Istituto di Psichiatria, Universita di Roma, Viale Universita, 30, I-00185 Roma, Italy **The prolactin response in patients receiving neurolep-**

tic therapy. The effect of fluphenazine decanoate. Progress in Neuro-Psychopharmacology. 5(1):69-77, 1981.

Increases in plasma prolactin (PRL) induced by 50mg fluphenazine decanoate (FD) were studied in three groups of male schizophrenic patients. The increase in plasma PRL was higher in patients who had never been treated with neuroleptic drugs than in those who had been treated with neuroleptics for at least 2 years or in those who had discontinued neuroleptic therapy for at least 3 months after treatment for at least 1 year. The PRL response did not correlate with psychopathological changes and extrapyramidal side-effects and did not appear to be a useful tool in predicting appropriate FD dosage. 14 references. (Author abstract modified)

004319 Duran, Eduardo; Schilkrut, Raul; Ercilla, Ramiro; Birkner, Rosa. Depto. de Psiquiatria y Salud Mental, Facultad de Medicina Sur, Universidad de Chile, Santiago, Chile **/Administration of flunitrazepam in electroconvulsive therapy./** Medicacion con flunitracepam en terapia electroconvulsivante. Acta Psiquiatrica y Psicologica de America Latina. 26(4):300-307, 1980.

Flunitrazepam, a benzodiazepine used as an anesthetic in major and minor surgery, was administered in 241 instances of electroconvulsive therapy (ECT) on 28 psychotic (primarily schizophrenic) patients. Results show that flunitrazepam induced deep sleep in 94.6% of the patients within 5 minutes. The required dosage was between 2 and 4mg. The drug did not inhibit the convulsion. There were no significant changes in pulse, arterial pressure, or respiration. Post-ECT agitation appeared in 0.82% of the subjects. Combined therapy with neuroleptics and lithium did not modify the effect of flunitrazepam. Increased tolerance did not develop after successive doses. The use of this drug avoids some of the problems associated with other anesthetics. Flunitrazepam should be used with older or high-risk patients who need ECT. 37 references. (Journal abstract modified)

004320 Elizur, A.; Levy, A.; Lahav, M.; Blum, I. Shalvata Psychiatric Center, Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel **Preliminary trial of clonidine treatment in two patients suffering from chronic schizophrenia.** Communications in Psychopharmacology. 4(6):507-517, 1980.

Clonidine was administered to two schizophrenic patients in a preliminary single-blind study. The first patient, whose initial psychopathology was that of retardation, crying, and withdrawal, showed a marked worsening of his condition after the administration of 5mcg clonidine per os. His blood pressure rose to 170/120 and his pulse rate to 120/minute. He became tense, hostile, aggressive, and totally preoccupied with auditory hallucinations. In the other patient, whose initial symptoms were maniform, clonidine had a marked, but transitory, beneficial effect. The significance of the differential effect of clonidine treatment in the two patients is discussed. 22 references. (Author abstract)

004321 Emrich, H. M.; Hollt, V.; Bergmann, M.; Kissling, W.; Schmid, W.; Zerssen, D. V.; Herz, A. Max-Planck-Institut fur Psychiatrie, D-8000 Munchen 40, West Germany **Plasma levels of beta-endorphin under chronic neuroleptic treatment in schizophrenic patients: failure of naloxone to counteract curative effects of neuroleptic drugs.** Advances in Biochemical Psychopharmacology. 22:489-502, 1980.

Plasma levels of beta-endorphin were assessed in schizophrenic patients during chronic neuroleptic treatment, and the effects of the specific opiate antagonist naloxone on neuroleptic actions were evaluated. All patients were treated with cataleptogenic neuroleptic drugs (haloperidol, perphenazine, benperidol). Naloxone failed to counteract the antipsychotic action of cataleptogenic antischizophrenic therapy. It is concluded that the curative action of neuroleptics is apparently not exerted via an endorphinergic mechanism. Therefore, the activation of endorphins induced by cataleptogenic antischizophrenic drugs perhaps constitutes an epiphenomenon of the therapy and may not be the causative factor underlying the beneficial effects of neuroleptic therapy. 18 references.

004322 Emrich, H. M.; Zaudig, M.; Kissling, W.; Dirlich, G.; van Zerssen, D.; Herz, A. Max-Planck Institut for Psychiatrie, Kraepelinstrasse 10, D-8000 Munchen 40, West Germany **Des-tyrosyl-gamma-endorphin in schizophrenia: a double-blind trial in 13 patients.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(5):290-298, 1980.

A double-blind placebo controlled cross-over investigation of the possible antipsychotic action of (des-Tyr1)-gamma-endorphin (DT-gamma-E), a nonopioid derivative of gamma-endorphin, was undertaken in 13 schizophrenic patients. The Ss were suffering from either chronic or acute, frequently relapsing schizophrenia and displayed persistent productive symptoms (hallucinations and acute delusions). Two successive double-blind injection treatment periods of 4 days followed 1 day of single-blind injection of placebo (4 days with i.m. injections of 2mg DT-gamma-E prededed 4 days of placebo injections or vice versa). Clinical data concerning each patient's age, sex, diagnosis, target symptoms, neuroleptic treatment, and the percentage of changes in symptomatology after treatment were analyzed. Psychopathological evaluation was performed twice daily by using the Inpatient Multidimensional Psychiatric Scale and an eight point scale for estimating the special target symptoms. Results indicate that the placebo and DT-gamma-E produce a reduction in symptomatology of an approximately equal magnitude, and the hypothesis of an antipsychotic efficacy of DT-gamma-E in treating chronic schizophrenic patients is not supported. In a subgroup of acute schizophrenic patients, some therapeutic action of DT-gamma-E was evidenced. 12 references. (Journal abstract modified)

004323 Gardos, George; Cole, Jonathan O.; LaBrie, Richard A. West-Ros-Park Mental Health Center, Cottage '1, 591 Morton St., Boston, MA 02124 **A twelve-year follow-up of the NIMH-PRB high dose chlorpromazine study of chronic schizophrenics -- implications for deinstitutionalization. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-32675, 1979. 51 p.

Results of a 12 year followup study of outcome in schizophrenics with established chronicity, a subject of particular interest in light of the controversy over their deinstitutionalization, are presented. Long-term outcome data, including repeated measures of symptoms and social adjustment were obtained from 124 patients who entered the drug phase of an original study on the use of chlorpromazine in the long-term management of the disorder. Measures included the Discharge Readiness Inventory, the Inpatient Multidimensional Psychiatric Scale, the Side Effects Checklist, and the Global Assessment Scale. At the 12 year followup, 90 of the 124 patients were contacted. The overall psychosocial adjustment in these Ss was disappointing. Outcome of the typical patient at followup was characterized as being markedly ill, receiving high doses of antipsychotic drugs, being unemployed, and showing poor social skills. Outcomes for patients placed in nursing homes were no better than for those remaining on hospital wards, while cooperative apartments seemed to be the best setting for these chronic mental patients. Family care patients occupied an intermediate position insofar as outcome was concerned. Particularly striking were the severe psychotic symptomatology, belligerence, poor social adjustment, and marked movement disorders, specifically restlessness, that were evidenced in the sampled Ss. 29 references.

004324 Goldstein, Allan L.; Rossio, Jeffrey; Kolyaskina, Galina I.; Emory, Lee E.; Overall, John E.; Thurman, Gary B.; Hatcher, Janelle. Dept. of Biochemistry, George Washington University School of Medicine, Washington, DC 20037 **Immunological components in schizophrenia.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 249-267).

Studies which would indicate that chlorpromazine (CPZ) by itself is a potent immunosuppressive agent, both in vitro and in vivo, in murine systems are summarized. The results of a clinical study, which indicate that a significant immunological imbalance exists in some patients with schizophrenia, are reported. These differences include abnormal lymphocyte responsiveness to selected mitogenic lectins and the presence in the serum of a cytotoxic factor(s) directed against murine thymocytes. The studies indicate that during a 28 day chemotherapy trial of CPZ there was a tendency towards normalization of T-cell responses and a significant decrease in serum cytotoxicity. Specific recommendations for new approaches to study immunologic and virologic components are presented, and questions which should be investigated to obtain information regarding the role of viruses and the immune system in the schizophrenic process are identified. A discussion of the paper follows. 38 references. (Author abstract modified)

004325 Gross, G.; Huber, G.; Schuttler, R. Huber: Universitats-Nervenklinik, D-5300 Bonn-Venusberg, West Germany /**The effect of long-term maintenance therapy on schizophrenic patients using somatotherapeutic measures.**/ Die Beeinflussung des Langzeitverlaufs schizophrener Krankheiten durch somatotherapeutische Massnahmen. Psychiatria Clinica. 13(3-4):179-192, 1980.

Evidence is presented in support of the effectiveness of long-term neuroleptic medication in schizophrenia, with emphasis on the great variability of course and outcome beyond the 3 year followup. Although some anamnestic and clinical progress was noted, it is contended that a reliable individual prognosis is not possible at disease onset. Initially phasic courses with complete remission of the early psychotic features are seen as possibly leading nevertheless to residual syndromes, while chronic persistent psychoses can demonstrate permanent remission. Observations are made on the favorable outcome following long-term treatment in some cases of catastrophic schizophrenia, the significantly less favorable outcome for patients whose disease began prior to the era of psychopharmacological drugs, and the more frequent occurrence of complete remission in patients with preacute and acute onsets of psychosis who received early treatment during the prodromal stage. The finding of a higher rate of patients with mixed residual states (at the expense of residual states) with long-term neurolepsy is seen as suggesting that long-term medication is responsible for the partially pharmacogenic change in symptomatology of schizophrenia insofar as it causes or favors a shift from the typical syndromes to the mixed residual states brought about by a potential reduction in symptoms. 29 references. (Journal abstract modified)

004326 Halperin, David A. 120 Central Park South, New York, NY 10019 Bulletin of the American Academy of Psychiatry and Law. 8(2):175-178, 1980.

A case report is presented which illustrates some of the difficulties which may arise in disclosure of information in accordance with the doctrine of informed consent. The doctrine stipulates that the physician must inform the patient of the consequences of a particular procedure and the side-effects of a particular medication. In the present case, a paranoid schizophrenic outpatient, maintained for 3 years on chlorpromazine, refrained from having children because of concerns about possible tetragenic side-effects of his medication. While the source of this misinformation was never pinpointed, the patient's misinterpretation of information about side-effects seemed to represent his general suspiciousness of the establishment in general. In this case the patient concealed his fantasies about medication from the treating physicians because of his treatment, such consent, was misinformed. Solutions to dilemmas involved in steering a course between underinformation and overexplication, and its possible negative effects, are outlined. 4 references.

004327 Hollister, Leo E.; Davis, Kenneth L.; Berger, Philip A. V.A. Medical Center, Palo Alto, CA 94304 **Apomorphine in schizophrenia.** Communications in Psychopharmacology. 4(4):277-281, 1980.

Studies of the utility of apomorphine in schizophrenia are described, and the idea of selective presynaptic receptor blockage as an approach to treating schizophrenia is discussed. Apomorphine in high doses given orally aggravated the psychotic symtoms of schizophrenic Ss, even though they continued treatment with previously effective doses of neuroleptics. At low doses, apomorphine failed to augment the beneficial effects of antispsychotic drugs. It is concluded that attempts to manage schizophrenia by selective blockade of presynaptic dopamine receptors may be difficult and may have limited clinical usefulness. 11 references. (Author abstract modified)

004328 Husser, J. Rheinische Landesklinik Koln, Koln, West Germany /**The treatment of chronic schizophrenic patients: an interview with Dr. J. Husser.**/ Die Behandlung chronisch schizophrener Patienten. Neurologie und Psychiatrie fur die Praxis. 6(3):156-157, 160, 1980.

The treatment of chronic schizophrenic patients is discussed. The progress made in the pharmacological sector and the development of potent neuroleptics have led to more rapid rehabilitation of these patients and briefer inpatient stays in clinics. Nevertheless, chronic schizophrenic patients are reinstitutionalized. The solution lies in finding a reliable residual safeguard following remission of symptoms as well as in promoting patients as suitable halfway house residents to facilitate their reintegration into society. The usual outpatient practice is to combine administration of long-term neuroleptics with social therapy and psychotherapy.

004329 Kolakowska, Tamara; Fraser, Sheila; Franklin, Michael; Knox, Jean. University of Oxford, Dept. of Psychiatry, Littlemore Hospital Research Unit, Littlemore Hospital, Oxford OX4 4XN, England **Neuroendocrine tests during treatment with neuroleptic drugs: I. Plasma prolactin response to chlorpromazine challenge.** Psychopharmacology. 72(3):283-285, 1981.

Plasma prolactin (PRL) levels were measured after a challenge dose of chlorpromazine (CPZ, 50mg) in 21 schizophrenics during neuroleptic treatment. In eight patients on low daily doses of neuroleptics, the challenge dose of CPZ elicited a rise in PRL levels beyond that induced by neuroleptic treatment. The challenge dose produced no change in plasma PRL in some patients, but an increase in PRL could be induced by increasing the challenge dose or increasing the daily dose of neuroleptics. It is concluded that the PRL rise after 50mg CPZ may identify patients whose PRL response to current neuroleptic treatment is submaximal. However, the absence of a PRL increment after the challenge dose may not indicate exactly that the baseline level is already maximal. 9 references. (Author abstract modified)

004330 Krupenina, L. B.; Prokhorova, I. S. Moskovskiy NII psikhiatrii, Ministerstva zdravookhraneniya RSFSR, Moskva, USSR /**Clinical and biochemical correlations in abrupt discontinuation of psychopharmacotherapy.**/ Kliniko-biokhimicheskiye sootnosheniya pri odnomomentnoy otmene psikhofarmakoterapii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(3):406-412, 1981.

Clinical and biochemical correlations following abrupt discontinuation of psychopharmacotherapy were studied in 26 patients (20 to 60 years old) with periodic and simple schizophrenia with a duration of 1 to 15 years. All the patients had received intensive psychopharmacotherapy, but without sufficient effect. Pharmacotherapy was discontinued abruptly. Before and after discontinuation of pharmacotherapy, the levels of adrenaline, noradrenaline, serotonin, and acetylcholine in the blood were determined, as well as the content of adrenaline, noradrenaline, dopamine, and vinylmandelic, homovanillic, and 5-hydroxyindoleacetic acids in the urine. A control group of 20 healthy people also was examined. Results indicate that an individualized therapeutic approach to different variants of paroxysmal schizophrenia is necessary, since the metabolism of biogenic amines in patients with periodic and simple schizophrenia is different. 20 references. (Journal abstract modified)

004331 Ladisich, Walter. Forschungstelle fur Psychopathologie und Psychotherapie, Max-Planck-Gesellschaft, Kraepelinstrasse 10, D-8000 Munchen 40, West Germany **Effects of Althesin in psychotherapy of schizophrenics: preliminary report.** Acta Psychiatrica Belgica. 80(4):445-451, 1980.

The use of Althesin in conjunction with psychotherapy for schizophrenics is discussed. Six patients were injected with Althesin in subhypnotic dosage prior to psychotherapy. The schizophrenics were nonresponsive to neuroleptics and had not benefitted much from psychotherapy. An analysis of the speech content of the therapy session of two Ss with the Gottschalk-Gleser method indicated that there is reduced hostility during Althesin sessions. Anxiety, however, was influenced less by Althesin administration. Two Ss' self-rated scores on a well-being scale indicated a beneficial effect of Althesin. Negative feelings decreased and patients appeared to be more assertive. 10 references. (Journal abstract modified)

004332 Langer, G.; Puhringer, W. Psychiatrische Universitats-Klinik, Abt. fur Psychiatrie, A-1097 Wien, Austria **Haloperidol and droperidol treatment in schizophrenics: clinical application of the** Acta Psychiatrica Belgica. 80(5):574-583, 1980.

To examine the relationships among neuroleptic treatment using haloperidol or droperidol, plasma prolactin response, suppression of neuroleptic-induced prolactin evaluation by dopamine infusion, and psychopathological change, longitudinal studies were made of four schizophrenic patients. A constant infusion of dopamine hydrochloride in the dose range of 15mcg/mn to 60mcg/mn was found to suppress prolactin elevation due to high dose neuroleptic maintenance medication. When the phenomenon was further investigated in another schizophrenic patient, a high test/retest reliability reproducibility for dopamine's suppressive effect on neuroleptic-induced elevated prolactin levels was found. In most instances, droperidol sharply raised plasma prolactin levels; however, in two patients two infusions did not elevate prolactin concentration. Despite the very high neuroleptic potency of droperidol (100mg given intravenously), not every infusion ameliorated schizophrenic psychopathology. Results are discussed in terms of the relationship between treatment response and prolactin response. 7 references. (Author abstract modified)

004333 McEvoy, Joseph P.; Berney, Stuart; Wilson, William H.; Ban, Thomas A.; Guy, William. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **A double-blind comparison of three dosages of flutroline (CP-36,584) in the treatment of schizophrenia.** International Pharmacopsychiatry. 15(5):318-324, 1980.

Therapeutic and adverse effects of three dosages (1, 20, and 100mg daily) of flutroline, a new gamma-carboline with a preclinical pharmacological profile similar to active neuroleptic agents, were compared in a double-blind clinical trial in 25 newly admitted schizophrenic patients. Therapeutic effects and extrapyramidal signs were seen at the 20 and 100mg daily dosages, but not at the 1mg dosage. Serum prolactin levels were significantly elevated only at the 100mg daily dosage. It is noted that for some patients, the therapeutic dosage of flutroline may lie above 20mg daily. While patients who developed elevation of serum prolactin level were significantly more likely to develop extrapyramidal signs, neither the occurrence of elevations of serum prolactin level nor the occurrence of extrapyramidal signs were significantly related to therapeutic response. 5 references. (Author abstract modified)

004334 Odejide, A. O. Dept. of Psychiatry, University College Hospital, Ibadan, Nigeria **Prevalence of persistent abnormal involuntary movements among patients in a Nigerian long-stay psychiatric unit.** International Pharmacopsychiatry. 15(5):292-300, 1980.

Patients in a Nigerian chronic psychiatric patients' unit (N=226) were examined for the evidence of abnormal involuntary movements. The disorder was found in 21 (9.3%) of the patients. The prevalence rate was higher among the females (14.5%) than among males (7%). All 21 patients had the diagnosis of schizophrenia. Also, they were found to be of an older age group than the total population. In comparison with a control group, the development of persistent abnormal involuntary movement was found not to be related to the daily dose of neuroleptic drugs administered or to the duration of the illness. It is concluded that the disorder is an idiosyncratic reaction. 22 references. (Author abstract modified)

004335 Panteleyeva, G. P.; Minsker, E. I.; Tsirkin, S. Yu.; Belyayev, B. S.; Lukanina, S. K. Institut psikhiatrii AMN SSSR, Moskva, USSR **/The use of clinical and pharmacokinetic criteria in forecasting the efficacy of therapy in schizophrenia./** Mesto klinicheskikh i farmakokineticheskikh parametrov v prognoze effektivnosti terapii shizofrenii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(5):748-754, 1980.

Clinical and pharmacokinetic criteria were developed to predict the efficacy of chlorpromazine in 25 patients with schizophrenia of different degrees of progression. Results show that the most informative clinical criteria were: the disease course, the structure of the prevalent syndrome, a relatively low level of negative personality changes, alternating affective disorders in the initial stage of the disease, and the development of the remental state after a single control dose of chlorpromazine. Results also show that the most informative pharmacokinetic criteria were the half-life of the drug and the penetration rate from the intestine into the blood. 11 references. (Journal abstract modified)

004336 Paykel, E. S. Dept. of Psychiatry, St. George's Hospital Medical School, London, S.W. 17, Australia **Psychopharmacological and social aspects of schizophrenia: recent developments.** Australian and New Zealand Journal of Psychiatry. 14(4):241-247, 1980.

Schizophrenia is considered with respect to pharmacological and psychosocial interactions. Substantial evidence is provided which suggests that biological factors, such as genetic and neurotransmitters, are involved in the etiology of schizophrenia, although their precise nature is uncertain. Environmental factors such as a possible virus contribution and early social conditions are considered, and studies of the recent social environment have been found to be most influential, especially those concerning life-even's proximate to relapse and the extreme sensitivity of the chronic schizophrenic to expressed emotion. It is suggested that social therapies and psychotherapies can provide only an additive benefit in conjunction with drugs. This provides a powerful argument for a combined approach. 53 references.

004337 Psaras, M.; Zissis, N. P.; Mouzakis, D.; Lyketsos, G. Zissis: 39, Mousson St., Pal. Phaleron, Athens, Greece **Mobilization of refractory chronic schizophrenics with haloperidol.** International Pharmacopsychiatry. 15(3):180-185, 1980.

Adequate high doses of haloperidol, averaging 100mg/day, were administered for 16 weeks to 24 chronic schizophrenics who were refractory to standerd antipsychotic treatment in an attempt to mobilize and release them from the hospital. At the end of the period, three patients were evaluated as able to leave the hospital, while 87% were subjectively evaluated as improved. High doses of haloperidol did not correlate with a higher incidence of unwanted effects. On the contrary, antiparkinson treatment was discontinued or decreased in 14 patients. It is concluded that nonresponsive chronic schizophrenics can profit from adequate high doses of haloperidol. 13 references. (Author abstract modified)

004338 Rao, V. A. Rama; Bailey, J.; Bishop, M.; Coppen, A. Coppen: MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey KT19 8PB, England **A clinical and pharmacodynamic evaluation of sulpiride.** Psychopharmacology. 73(1):77-80, 1981.

In a double-blind study, the therapeutic efficacy of sulpiride was compared to that of haloperidol, an established neuroleptic agent. A total of 30 female patients with a diagnosis of chronic schizophrenia were initially stablized on the dosage of haloperidol which produced optimum therapeutic response when given once or twice daily. The patients were then randomly allocated to receive either sulpiride or haloperidol over a period of 12 weeks. Plasma drug concentrations and prolactin levels were determined. Clinical effects were evaluated by Brief Psychiatric Rating Scale (BPRS), Wing Rating Scale, and Extrapyramidal Symptoms Rating Scale (EPS). A standardized side-effects checklist was used. Treatment with sulpiride was associated with a significant rise in plasma prolactin level, but paradoxically, these patients had significantly reduced extrapyramidal symptoms. No significant correlation was found between plasma sulpiride concentration and prolactin level or any of the clinical variables. Results confirm the antipsychotic activity of sulpiride. 23 references. (Author abstract modified)

004339 Shestakov, S. V. Kafedra psikhiatrii, Voronezhskiy meditsinskiy institut, Voronezh, USSR **/The use of sodium nucleinate in the treatment of schizophrenic patients./** Ispol'zovaniye nukleinata natriya v terapii bol'nykh shizofreniyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(5):623-627, 1979.

A total of 142 patients (80 men and 62 women, 19 to 60 years old) with progressive forms of schizophrenia with pronounced symptomatology were treated with sodium nucleinate and other substances. Most of the patients had been suffering from the illness for over 10 years. Sodium nucleinate alone was given to 17 of the patients; 85 received it along with psychotropic substances such as aminazine and trifluoperazine; and 40 received neuroleptics along with a therapeutically indifferent substance instead of nucleinate. The dynamics of some indices of nonspecific reactivity were observed during treatment. Yeast sodium nucleinate was found to promote a softening and reversal of some deficital symptoms, mainly in the emotional volitional sphere, and to decrease the threshold of sensitivity to neuroleptics. When remission occurred, the immunological indices returned to normal. 19 references. (Journal abstract modified)

004340 Smulevich, A. B.; Bosov, A. M.; Dubnitskaya, E. B.; Izmaylova, L. G. Insitut psikhiatrii AMN SSSR, Moskva, USSR **/The problem of psychopharmacotherapy of slowly progressive hypochondriacal schizophrenia./** K probleme psikofarmakoterapii maloprogredientnoy ipokhondricheskoy shizofrenii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(11):1583-1587, 1979.

The psychopharmacological aspect of nonpsychotic hypochondriacal conditions in schizophrenia was studied in 155 patients (from 20 to over 60 years old) who were treated in one institution between 1976 and 1978. All the Ss suffered from slowly progressive schizophrenia. In most of the cases (139) this disease was of uninterrupted course, and only in 16 cases was it an attack-like process. The Ss were divided into three groups: neurosis-like hypochondria, physical sensations (pains), and rigid hypochondria. Results show that neither coma therapy nor the use of large doses of neuroleptics significantly reduced psychopathological symptoms. However, positive results were achieved with a combination of tranquilizers and small doses of neuroleptics. 23 references.

004341 Steiner, S. Niederosterreichisches Landeskrankenhaus fur Psychiatrie und Neurologie, Hauptstrasse 2, A-3400 Klosterneuburg, Austria **/The effect of an intensive course of neuroleptic drugs on schizophrenic patients and their subsequent course following the cessation of all neuroleptic medication./** Beeinflussung schizophrener Erkrankungen durch eine neuroleptische Intensivbehandlung und der weitere Verlauf nach Absetzen jeder neuroleptischen Medikation. Psychiatria Clinica. 13(3-4):165-178, 1980.

A group of 229 patients with schizophrenic or other paranoid illnesses (9 patients) were treated for about 14 weeks with intramuscular or intravenous injections of fluphenazine decanoate, and their subsequent course was monitored after 3 years. During the first 2 weeks, three injections of 250mg were given, followed by slowly lowering dosages at three weekly intervals. Ss also received tablets of procyclidine and 100mg to 150mg of amitriptyline p.o. After the initial intensive phase, Ss received an average of 145mg i.m. every 3 weeks. The findings at the 3 year followup confirm those from an earlier assessment which showed the rapid onset and stability of remission, the absence of relapses among patients who continued treatment, and the relative freedom from relapses among patients who did not continue to receive neuroleptic medication. The suggestion that the initial high dosage medication would have deleterious effects on the personality, producing robot-like or zombie-like behavior, was not confirmed. 3 references. (Journal abstract modified)

004342 Tegeler, Joachim; Lehmann, Erlo. Rheinische Landesklinik, Psych. Klinik, Universitatslinik Dusseldorf, Bergische Landstrasse 2, D-4000 Dusseldorf 12, West Germany **A follow-up study of schizophrenic outpatients treated with depot-neuroleptics.** Progress in Neuro-Psychopharmacology. 5(1):79-90, 1981.

Data from 78 schizophrenic patient attending an outpatient clinic were used to compare the efficacy of long-acting neuroleptics and short acting medication. Over a 5 year period, the readmission rate and duration of inpatient stay were significantly lower during treatment with depot neuroleptics than during treatment with short acting drugs. Demograhic data and therapeutic conditions that may have influenced these results are discussed. 14 references. (Author abstract modified)

004343 Vardi, J.; Flechter, S.; Oberman, Z.; Segal, R.; Shogan, G.; Haker, O. Dept. of Neurology and Chemical Pathology, Medical School Tel Aviv University, Tel Aviv, Israel **Plasma dopamine beta hydroxylase activity in chronic schizophrenic patients tested with single dose of 2-bromo-alpha ergocriptine (Parlodel).** Encephale. 7(1):95-103, 1981.

Plasma dopamine beta hydroxylase (DBH) activity was measured in six chronic schizophrenic patients. The six Ss received 7.5mg of bromocriptine and blood samples were taken at regular intervals for 3 hours. Two control groups were used: a group of six schizophrenics who received no bromocriptine and a group of five normal individuals who received 7.5mg of bromocriptine. Results show a significant increase in DBH activity in the Ss compared to the control groups. This might be explained by hypersensitivity models of presynaptic and postsynaptic receptors, and of agonist and antagonist properties of bromocriptine when acting on these receptors. 33 references. (Journal abstract modified)

004344 Zander, K. J.; Fischer, B.; Zimmer, R.; Ackenheil, M. Ackenheil: Psychiatrische Klinik der Universitat Munchen, Nussbaumstrasse 7, D-8000 Munchen 2, West Germany **Long-term neuroleptic treatment of chronic schizophrenic patients: clinical and biochemical effects of withdrawal.** Psychopharmacology. 73(1):43-47, 1981.

Clinical and biochemical effects of withdrawal from long-term neuroleptic treatment were studied in 17 chronic schizophrenic patients under neuroleptic treatment for 13 years. A 30 day drug withdrawal resulted in early relapse of four patients, slight deterioration of five patients, and slight amelioration in eight patients. No incidents of neuroleptic symptoms such as tardive dyskinesia occurred. Prolactin in plasma and cerebrospinal fluid (CSF), not being elevated under chronic treatment, decreased significantly after 30 days of withdrawal. Homovanillic acid and 3-methoxy-4-hydroxyphenylglycol in CSF ranged normally and did not change during withdrawal. In contrast, plasma noradrenaline was elevated and decreased after drug discontinuation. No unequivocal relationship between biochemical and psychopathological features was found. 42 references. (Author abstract modified)

004345 Zisook, Sidney; Click, Maurice A., Jr. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **Evaluations of loxapine succinate in the ambulatory treatment of acute schizophrenic episodes.** International Pharmacopsychiatry. 15(6):365-378, 1980.

The efficacy of loxapine succinate in treating acute schizophrenic episodes of outpatients was assesed with 138 acutely ill schirophrenic outpatients. The patients were treated with oral loxapine succinate for up to 4 weeks in nine open label studies, all of which shared an identical protocol. For most patients, a daily dose of 30mg to 80mg loxapine was observed to provide safe, effective, and relatively immediate symptomatic relief, and in most cases, it helped to keep acutely ill schizophrenic patients out of the hospital. Side-effects, which occurred in 95 patients, were mostly mild and controllable and consisted mainly of extrapyramidal effects. 56 references. (Author abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

004346 Al-Yassiri, M. M.; Bridges, P. K. Academic Unit for Clinical Psychopharmacology, Guy's Hospital Medical School, London SE1 9RT, England **Trazodone efficacy and safety in endogenous depression: a double blind comparison with imipramine.** Neuropharmacology. 19(12):1191-1193, 1980.

The efficacy and side-effects of trazodone and imipramine, given orally to a group of patients suffering from endogenous depression, were investigated in a double-blind study. Data from the 26 Ss in the 6 month study indicate that trazodone has antidepressant activity at least as potent as imipramine. Both drugs produced significant reduction in Wakefield Depression Scale and Hamilton Depression Scale scores. Trazodone seems to be well tolerated and to have less anticholinergic effects than imipramine. Dizziness and drowsiness are the main complaints of the patients on trazodone.

004347 Albarello, B. 1. Servizio Psichiatrico O. C. Borgo Trento, Vernona, Italy **/On the use of certain pharmacological categories in hysteria./** Sull'uso di alcune categorie di psicofarmaci nelle forme isteriche. Rivista di Neuropsichiatria e Scienze Affini. 26(2):103-113, 1980.

A biochemical interpretation of hysteria is proposed based on three case studies. In the first case, treatment of a 30-year-old woman with small dose of antidepressants was ineffective, and she returned to the clinic twice. She began to respond to average doses of tricyclic antidepressants, which improved her hysterical symptoms. A 23-year-old woman who rejected and would not care for her son showed little responsiveness to neuroleptic treatment. At her second admission, however, she was treated more successfully with increasing doses of antidepressants. Th third case involves a 54-year-old woman whose hysteria was induced by trauma and who recovered somewhat under a varied drug treatment program but was maintained on antidepressants alone. It is concluded that average doses of tricyclic antidepressants and small doses of benzodiazepines are most effective in the treatment of hysteria. Theories of hysteria are discussed. 17 references. (Journal abstract modified)

004348 Ananth, J.; Engelsmann, F.; Kiriakos, R. Allan Memorial Institute, Montreal, Quebec H3A 1A1, Canada **Evaluation of lithium response: psychometric findings.** Canadian Journal of Psychiatry. 25(2):151-154, 1980.

The usefulness of the MMPI in the prediction of lithium therapy response was investigated in 59 bipolar affective disorder patients, 39 of whom had no recurrences of manic-depressive illness and functioned at premorbid levels during 2 years of lithium treatment (responders) and 20 of whom had had psychotic episodes during this period despite adequate lithium serum levels (nonresponders). Nonresponders obtained higher scores on Psychopathic Deviate, Paranoid, and Mania Scales; while responders scored higher on the Hypochondriasis, Psychasthenia, and Social Introversion scales. Further work with pretreatment and posttreatment administration of the MMPI may provide additional and more definitive results. 5 references. (Author abstract modified)

004349 Asarch, Kenneth B.; Shih, Jean C.; Kulcsar, Agnes. School of Pharmacy, University of Southern California, 1985 Zonal Avenue, Los Angeles, CA 90033 **Decreased 3H-imipramine binding in depressed males and females.** Communications in Psychopharmacology. 4(5):425-432, 1980.

The high affinity binding of 3H-imipramine to platelet memberanes from 23 untreated depressed men and women and 16 normal men and women was studied. The maximal binding (Bmax) in the depressed groups, male as well as female, was signficiantly lower (20%) than in the normal groups, while the dissociation constants (Kd) were not significantly different. Neither Bmax nor Kd differed statistically between the sexes for either the depressed or normal subject groups. No significant correlations were found between age and either Bmax or Kd for any of the four S subgroups. A statistically significant correlation did exist, though, between the Bmax of all of the Ss and their respective dissociation constants. In addition, 3H-imipramine binding to platelet membranes remained unchanged during 2 weeks of daily therapy on the monoamine oxidase inhibitor, tranylcypromine. 9 references. (Author abstract)

004350 Ayd, Frank J, Jr. no address **Clinical depressions: diagnostic and therapeutic challenges.** Baltimore, Ayd Medical Communications, 1980. 228 p. $20.

A series of statements is presented by experienced clinicians on their concepts of depressions and their therapies. An overview of depression and its management is provided and covers the signs and symptoms of primary and secondary depression, depression in geriatric patients, alternatives to psychopharmacological methods, and techniques for initiating antidepressant drug therapy for outpatients. The overview is followed by a consideration of the social effects of depression, the depressed medical patient, and differentiating anxiety and depression. Depressive pseudodementia is covered as are the multiple facets of masked depression with an emphasis on the faciopsycho-myalgia syndrome. Acute chronic depression, the depressive personality, and a biopsychosocial model of depression are discussed. The postmarketing surveillance of maprotiline in Canada is included as an addendum.

004351 Ballus, C. Departamento de Psiquiatria y Psicologia Medica, Facultad de Medicina, Casanova 143, Barcelona 36, Spain **Pharmacotherapy for depression.** In: Kielholz, P., The general practitioner and his depressed patients. Bern, Switzerland, Hans Huber, 1981. 142 p. (p. 86-96).

Pharmacotherapeutic treatment of depression is discussed. Before treatment the depression must be classified nosologically as either psychogenic, endogenous, or somatogenic. Pharmacotherapy is primarily indicated in endogenous depressions, although they can play a role in psychogenic and somatogenic depressions. Selection of an appropriate antidepressant depends on phenomenological features and whether the clinical picture is predominantly characterized by depressive mood, anxious agitation, psychomotor retardation or functional disturbances. The antidepressants are classified as mood brightening, sedative anxiolytic, or drive enhancing. These include tricyclic antidepressants, tetracyclic antidepressants, antidepressants of other types, and monoamine oxidase inhibitors. The administration and dosage, side-effects, and contraindications of antidepressants are reviewed. 16 references.

004352 Baxter, Claude F.; Tachiki, Ken H.; Blaser, Steven M.; Bednar, Bryce R.; Gosenfeld, Lawrence F. Neurochemistry Laboratories, Sepulveda Veterans Administration Medical Center, Sepulveda, CA 91343 **Changes in blood plasma osmolality and status of mania.** Neurochemical Research. 6(1):47-53, 1981.

In hospitalized male manic patients, fluctuations in blood plasma osmolality over a period of months showed a significant inverse correlation with changes in mania rating scores. Successful treatment with lithium carbonate was correlated with increasing levels of plasma osmolality and with significant remission of manic symptoms. It is suggested that altered plasma osmolality is linked to changes in manic symptomatology through osmotically regulated metabolic changes in the CNS. 37 references. (Author abstract modified)

004353 Belmaker, Robert H. Jerusalem Mental Health Center, Ezrath Nashim, Jerusalem, Israel **Receptors, adenylate cyclase, depression, and lithium.** Biological Psychiatry. 16(4):333-350, 1981.

A clinical trial of the beta-2 adrenergic agonist, salbutamol (.25mg, intravenously) was conducted to test whether adrenergic receptor subsensitivity does occur during clinical antidepressant treatment. After 1 and 3 weeks oral salbutamol treatment, depression scores declined significantly in 11 depressed patients, while the plasma cyclic adenosine monophosphate (cAMP) response to intravenous salbutamol declined over 60%. The beta-adrenergic adenylate cyclase remained subsensitive 4 days after cessation of salbutamol therapy. Data are presented that lithium (Li), too, markedly reduces activity of beta-adrenergic adenylate cyclase in humans. The effect was evaluated by studying the effect of Li at therapeutic serum concentrations on plasma cAMP response to subcutaenous epinephrine. The Li effect is specific, since plasma cAMP response to glucagen was not inhibited. The plasma cyclic GMP response to subcutaneous epinephrine, suggested as a model for presynaptic alpha-noradrenergic mechanisms, is also partially inhibited by Li therapy. Since cAMP and cyclic GMP may be viewed as balancing substances, their interaction may provide a mechanism for Li's dual clinical effects in mania and depression. 60 references. (Author abstract modified)

004354 Bertoletti, Paolo. Ospedale S. Maria della Pieta, Roma, Italy **/Anxious-depressive syndrome. Clinical study of a new benzodiazepine, prazepam./** Sindromi ansioso-depressiva. Studio clinico su una nuova benzodiazepina, il prazepam. Lavoro Neuropsichiatrico. 66(3):53-59, 1980.

Twenty depressed patients between ages 25 and 40, whose illness was expressed in tension and other physical symptoms, were treated with prazepam (30 to 60mg, administered three times daily) for 3 months. Results show that patients' anxiety, tension, insomnia, and physical distress were reduced. Also, Ss' general condition and mood were improved. An undesirable sedative effect in three patients was eliminated by decreasing the dosage from 60 to 30mg daily. 8 references.

004355 Bogaert, M. G.; Rosseel, M. T.; Deberdt, R.; Vranckx, C. Heymans Institute of Pharmacology, University of Gent Medical School, De Pintelaan 135, B-9000 Gent, Belgium **Plasma levels of the cis- and trans-isomers of doxepin and desmethyldoxepin after administration of doxepin to patients.** Arzneimittel-Forschung. 31(1):113-115, 1981.

In depressed patients treated acutely or chronically with doxepin, a 15:85% mixture of cis-isomers and trans-isomers of N,N-dimethyldibenz(b,e)oxepin-delta11(6H)-3-propylamine, plasma levels of the cis-forms and trans-forms of doxepin and desmethyldoxepin were measured using a GLC method with a capillary column and a nitrogen detector. In two patients 50mg of doxepin were administered three times daily for 5 days, in nine patients plasma samples were taken every few days during the first weeks of treatment with 50mg t.i.d. of doxepin, and steady-state levels were obtained after 3 weeks of treatment in patients given 25mg t.i.d. of doxepin and in patients given 100mg of doxepin once daily. A gradual increase in the concentration of the products in the plasma was evident in the first days of doxepin administration. There is variation between patients in the steady-state concentrations of trans-doxepin and of cis-desmethyldoxepin and trans-desmethyldoxepin. cis-Doxepin levels always are very low. It is suggested that for studies of correlations between plasma levels and therapeutic and toxic effects of doxepin, the isomers of the parent compound and its metabolite should be measured separately. 8 references. (Journal abstract modified)

004356 Boutelle, W. E. V. A. Medical Center, Northampton, MA **Clinical response and blood levels in the treatment of depression with a new antidepressant drug, amoxapine.** Neuropharmacology. 19(12):1229-1231, 1980.

The divided dose regimen and the single daily dose administration of amoxapine were compared, and the relationship between clinical response and steady-state blood levels of amoxapine and its 8-OH metabolite in the treatment of depressed patients was assessed. Both divided dose and single daily dose administration of amoxapine were found almost equally effective in alleviating the depressed symptoms in various types of depressed patients. Overall incidences of adverse experiences were slightly different. Data concerning the correlation between clinical state and blood levels of amoxapine appear to support the original finding of Asberg, Cronholm Sjoqvist, and Tuck (1971). 5 references.

004357 Braccini, T.; Darcourt, G.; Corti, H.; Lapalus, P.; Lavagna, J.; Myquel, M. Hopital Pasteur, Service de Psychiatrie et de Psychologie medicale, F-06031 Nice Cedex, France **/Clinical significance of the erythroplasmatic ratio of lithium./** Signification clinique du rapport erythro-plasmatique du lithium. Acta Psychiatrica Belgica. 80(4):413-419, 1980.

Six hundred erythroplasmatic ratios of lithium in 67 Ss with affective disorders were studied. Ratio values during relapse phase were not significantly different than those values found during remission phases. The same was true for periods with neuroleptic treatment and phases without neuroleptic treatment. Ratio values were not noticeably modified by personality, sex, or the evolution of the disorder. However, the results indicate that the preventive effect of lithium is found primarily in Ss with high erythroplasmatic levels. 15 references. (Journal abstract modified)

004358 Briley, M. S.; Raisman, R.; Sechter, D.; Zarifian, E.; Langer, S. Z. Dept. of Biology Synthelabo LERS, 58, rue de la Glaciere, F-75013 Paris, France **(3H)-Imipramine binding in human platelets: a new biochemical parameter in depression.** Neuropharmacology. 19(12):1209-1210, 1980.

A preliminary study of (3H)imipramine binding sites in depressed patients is described, and the utility of (3H)imipramine binding in human platelets as a biochemical parameter in depression is discussed. Platelets of 16 untreated severely depressed women were found to possess significantly fewer binding sites than those of a control group of 21 normal women of the same ages. The affinity for (3H)imipramine was the same in the two groups. The possible relationship between this finding and mood is discussed. It is suggested that low platelet binding of (3H)imipramine may be an indication of a genetic predisposition to depression, thus remaining low even after the depression has passed. 10 references.

004359 Carroll, Bernard; Feinberg, Michael; Greden, John; Tarika, Janet; Albala, A.; Haskett, Roger; James, Norman; Kronfol, Ziad; Lohr, Naomi. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Standardization of the dexamethasone suppression test for the diagnosis of melancholia. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-28294, 1980.

A group of 368 psychiatric patients and 70 normal controls were studied with an overnight dexamethasone suppression test (DST) in order to standardize the test for the diagnosis of patients with melancholia (endogenous depression). Abnormal escape of plasma cortisol concentrations from suppression within 24 h after administration of dexamethasone occurred frequently in melancholic patients but rarely in other Ss. The optimal plasma cortisol criterion concentration above which a DST result may be considered abnormal, was 5mcg/dl. The optimal dose of dexamethasone was 1mg, which gave an overall test sensitivity double that obtained with a dexamethasone dose of 2mg, without loss of specificity. The most efficient schedule of blood sampling was the combination of samples obtained at 1,600 and 2,300 h postdexamethasone. These two blood samples detected 98% of the positive tests. The DST procedure identified melancholic Ss with a sensitivity of 67% and a specificity of 96%. The diagnostic confidence for melancholia of a positive DST result was 94%. Based on the plasma cortisol concentrations obtained only at 1,600 h postdexamethasone, there was no significant difference in the sensitivity observed among melancholic outpatients and inpatients. Abnormal DST results were not related significantly to age, sex, recent use of psychotropic drugs, or severity of depressive symptoms. It is concluded that there is extensive evidence which validates this practical test for the diagnosis of melancholia. 39 references. (Author abstract modified)

004360 Catlin, Don H.; Gorelick, David A.; Gerner, Robert H.; Hui, Ka Kit; Li, Choh Hao. Dept. of Pharmacology, University of California, Los Angeles, CA 90024 **Clinical effects of beta-endorphin infusions.** Advances in Biochemical Psychopharmacology. 22:465-472, 1980.

Clinical effects of beta-endorphin infusions were evaluated in eight depressed psychiatric inpatients and in four narcotic addicts maintained on methadone for at least 2 years. Intravenous administration of synthetic human beta-endorphin produces physiological and hormonal effects in man, with some suggestion of behavioral effects as well. These effects are pharmacological, rather than physiological ones, since they occurred at plasma concentrations several orders of magnitude greater than baseline levels of endogenous beta-endorphin. Results suggest that peripherally administered beta-endorphin may enter the CNS. It is suggested that beta-endorphin activates a different class of opiate receptors in man than it does in animals, and a different class than does morphine. 36 references. (Author abstract modified)

004361 Cazzullo, C. L.; Sacchetti, E.; Smeraldi, E. Institute of Clinical Psychiatry, University Medical School, Milan, Italy **Psychotropic drugs and their relationship with psychopathology of affective disorders.** Progress in Neurobiology. 3:25-38, 1979.

The relationship between the psychopathology of depressive behavior and the effectiveness of drugs affecting mood is discussed. Nonpsychological validation of diagnosis of primary affective disorders is considered. Predictability of the response to antidepressant drugs is covered. Factors involved in the effectiveness of long-term lithium treatment are examined. (Journal abstract modified)

004362 Checkley, S. A. no address **A neuroendocrine study of adrenoceptor function in endogenous depression.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):211-217, 1980.

Hormone responses to methylamphetamine were measured in patients with depressive illness and in control patients. The corticosteroid response to methylamphetamine was significantly less in 20 patients with endogenous depression than in six patients with reactive depression, eight patients with other functional psychoses, and 10 patients with other psychiatric illnesses. The same response was also less in 10 patients when they were depressed as compared to when they had recovered. In contrast, growth hormone responses to methylamphetamine were similar in all the groups which were tested. It is suggested that patients with endogenous depression have a defect at some central alpha-adrenoceptors. A panel discussion of these findings is appended. 27 references. (Author abstract modified)

004363 Cookson, J. C.; Silverstone, T.; Besser, G. M.; Williams, S. Academic Unit of Human Psychopharmacology, Medical College of St. Bartholomew's Hospital, Ritson Road, London E8 1DF, England **Plasma corticosteriods in mania: the effects of pimozide.** Neuropharmacology. 19(12):1243-1244, 1980.

Plasma corticosteroid levels of six manic patients were monitored for 2 weeks to determine how abnormalities in these levels respond during treatment with pimozide. Venous blood samples were taken at 09:00, 18:00, and 24:00 hours on the day before medication started and on days 3, 7, and 14 of medication. Clinical state was assessed using the eight item rating scale of Pettersen, Fyro, and Sedvall (1973). The mean corticosteroid levels before treatment were raised outside the normal range, with blunting of the circadian rhythm. During the 2 week treatment period, clinical ratings and plasma corticosteroid levels reflected gradual improvement. The effectiveness of pimozide in lowering towards normal the raised corticosteroid levels of these patients, suggests that the mechanisms underlying the raised levels of mania differ at least in part from the mechanisms underlying the raised cortisol levels of patients with endogenous depression. 10 references.

004364 Coppen, A.; Wood, K. M. no address **Peripheral serotonergic and adrenergic responses in depression.** Acta Psychiatrica Scandinavica 61(Suppl. 280):21-28, 1980.

Peripheral serotonergic and adrenergic responses were investigated among depressed patients following a 6 week period of tricyclic antidepressant administration using three assessment procedures: 1) platelet serotonin (5-HT) uptake; 2) tyramine, noradrenaline, and phenylephrine dose/pressor response test; and 3) plasma concentration of amitriptyline and nortriptyline. The capacity of transport of 5-HT through the platelet membrane is reduced significantly in depressive patients. The concentration of amitriptyline in the plasma is related positively and significantly to the inhibition of uptake of 5-HT by blood platelets of depressed patients, but there is no significant correlation between platelet 5-HT uptake inhibition and clinical improvement. The phenylephrine, tyramine, and noradrenaline pressor tests all show a result that is consistent with increased sensitivity of the peripheral alpha-adrenoreceptors in patients with depression. All the tests indicate changes (decreases in sensitivity) resulting from the use of amitriptyline. A discussion of the findings is appended. 23 references.

004365 Faravelli, C.; Marchetti, G.; Benvenuti, P.; Cabras, P. L. Clinica Psichiatrica, Universita di Firenze, Firenze, Italy / **Lithium in the prophylaxis of recurrent affective disorders (effectiveness of low plasma levels and predictors to clinical response).**/ Il litio nella prevenzione delle turbe cicliche dell'affettivita (efficacia dei bassi livelli plasmatici e fattori di previsione dell'esito della terapia). Rivista di Patologia Nervosa e Mentale. 101(6):261-271, 1980.

Results are presented from treating 38 patients with recurrent affective disorder with lithium carbonate for a period of 3 to 8 years. Good response was observed in 24 Ss, who had a decrease of at least 50% in recurrences during the treatment period as compared with the period preceding it. This improvement was obtained in spite of the fact that plasma lithium was maintained within 0.40 to 0.80 mEq/l, a range lower than recommended. Ss whose plasma lithium fell below 0.40 had significantly increased relapses. No marked toxic effect was recorded. Some factors (bipolar illness, typical symptom pattern, and family history of affective disorder) were associated with a favorable outcome. The absence of these factors, however, did not predict a poor response in more than 40% of the cases. It is concluded that it is worthwhile to start a lithium treatment whenever a diagnosis of recurrent affective disorder is made. 19 references. (Journal abstract modified)

004366 Fink, Max. Dept. of Psychiatry and Behavioral Science, School of Medicine, State University of New York, Stony Brook, NY 11794 **Convulsive and drug therapies of depression.** Annual Review of Medicine: Selected Topics in the Clinical Sciences. 32:405-412, 1981.

Selected studies of convulsive and drug therapies of depression are reviewed, and the safety and efficacy of electroconvulsive therapy (ECT) are compared with those of antidepressant drugs. It is noted that antidepressant drugs and ECT are both effective therapies of endogenous depression, and some antidepressant and anxiolytic drugs may influence aspects of neurotic depression favorably. While ECT is clearly more effective than tricyclic antidepressants and monoamine oxidase inhibitors, the additional difficulty in administering ECT, the public image of its special hazards, and the ease of administering drug therapies make their use generally preferred. There are special conditions, however, such as the severity of illness, the risk of death by inanition or suicide, and medical complications (including pregnancy) that lead the prudent physician to recommend ECT. 71 references. (Author abstract modified)

004367 Gershon, Samuel; Goodnick, Paul J. Dept. of Psychiatry, Wayne State University, Detroit, MI 48202 **Lithium use in affective disorders.** Psychiatric Annals. 11(4):38-40, 42-43, 47-48, 53, 55-57, 1981.

The use of lithium in the treatment of affective disorders and of schizophrenia, and the side-effects associated with lithium therapy are discussed. Lithium has been shown to have a very specific effect on mania. Comparisons between lithium therapy and the use of chlorpromazine are reviewed. Chlorpromazine controls motor activity more rapidly, but total normalization occurs with lithium whereas return to normal motor activity is slower, less consistent, and less complete in patients receiving chlorpromazine. Lithium exerts a more complete and more specific effect on the entire range of behavior found in mania, bringing about a more complete recovery even though it is much slower in producing clinical results when first administered. Studies on the effectiveness of lithium as an antidepressant are reviewed. There are four schools of thought on the use of lithium in the treatment of schizophrenia: that lithium is actually harmful because of the possibility of toxicity to the central nervous system, that schizophrenic patients who respond to lithium are actually atypical manic-depressives, there is a subgroup of true schizophrenics who respond favorably to lithium, lithium may be useful when used in combination with another drug. Further research is needed to pinpoint the efficacy of lithium in treating recurrent mania, manifest depression, and schizophrenia, but the trend of investigation to date indicates that lithium may be useful in treating at least important subgroups of such patients. 54 references.

004368 Glassman, Alexander H. Dept. of Psychiatry, Columbia University College of Physicians and Surgeons, New York, NY 10032 **Blood-level measurements of tricyclic drugs as a diagnostic tool.** Psychiatric Annals. 11(4):14-15, 19-23, 1981.

The use of laboratory determinations of plasma levels of tricyclic drugs of patients under the care of a psychiatrist for depression is discussed. Studies using imipramine are reviewed. Individuals given identical dosages of tricyclic antidepressants can develop quite different plasma concentrations of the drug. Retrospective findings indicate that almost one out of every five patients 65 years of age or older receiving imipramine has an orthostatic hypotension that is serious enough to cause treatment to be altered or discontinued. Determinations of plasma levels of tricyclics can be useful for refractory patients, for patients with adverse reactions, and for patients with heart disorders. Plasma level determinations are useful to the clinician in determining a therapeutically effective dosage, in increasing clinical efficacy and in providing a better understanding of the drug's toxicity. 14 references.

004369 Goodnick, Paul J.; Fieve, Ronald R.; Meltzer, Herbert L.; Dunner, David L. Dept. of Psychiatry, Wayne State University, Veterans Administration Medical Center, Southfield and Outer Drive, Allen Park, MI 48101 **Lithium elimination half-life and duration of therapy.** Clinical Pharmacology and Therapeutics. 29(1):47-50, 1981.

The elimination half-life of lithium carbonate in red blood cells, plasma, and urine were measured in 30 patients hospitalized for primary affective disorder. The half-life values were lowest in patients on their initial course of lithium (1.12, 1.28, and 1.22 days for urine, plasma, and red blood cells, respectively). Patients on lithium for less than 1 year had intermediate values (1.85, 1.65, and 1.75 days), and those on lithium for more than 1 year had the longest values (2.40, 2.43, and 2.24 days). Results indicate that lithium may stimulate the production of an endogenous regulator of lithium efflux, which may be an important factor in planning long-term lithium prophylaxis. 27 references. (Author abstract modified)

004370 Gram, L. F. no address **Pharmacokinetics and clinical response to tricyclic antidepressants.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):169-180, 1980.

The status of clinical research in plasma monitoring of the tricyclic antidepressants is outlined, and methodological problems and diagnostic issues in plasma monitoring are discussed. It is noted that although plasma levels of tricyclic antidepressants are an important variable determining clinical effect, other variables, particularly diagnostic selection of patients, are equally important determinants of clinical outcome. Plasma level/effect relationships have been established reasonably well for only two tricyclic antidepressants, nortriptyline and imipramine. It is concluded that by having the various methodological factors better elucidated and by having more practical clinical data on plasma level monitoring available, it should be possible to conduct cost/benefit analyses that would permit proper recommendations for the more general use of plasma level monitoring of tricyclic antidepressants in future clinical practice. A panel discussion of this paper is appended. 31 references.

004371 Helmchen, H. Psychiatrischen Klinik der Freien Universitat, Berlin, Eschenallee 3, D-1000 Berlin 19, West Germany **Interactions between antidepressants and other drugs.** In: Kielholz, P., The general practitioner and his depressed patients. Bern, Switzerland, Hans Huber, 1981. 142 p. (p. 97-104).

Various forms of polypharmacy involving antidepressants are reviewed for three sets of circumstances: multimorbidity, long-term medication in normal subjects, and self-medication. The interactions between antidepressants and other drugs in cases of hypertension, cardiovascular disorders, and diabetes are discussed. The use of oral contraceptives and antidepressants are also considered. It is argued that complications due to polypharmacy arise under the following circumstances: 1) failure to use caution in adapting dosages to the blood concentrations required for therapeutic purposes; 2) failure to carefully observe and monitor the patient; and 3) failure to interrupt drug treatment frequently enough in order to reassess the clinical picture. 13 references.

004372 Holmberg, G. Psykiatriska kliniken, Danderyds Sjukhus, S-18203, Danderyd 3, Sweden **Long-term treatment for depression.** In: Kielholz, P., The general practitioner and his depressed patients. Bern, Switzerland, Hans Huber, 1981. 142 p. (p. 117-122).

Long-term use of prophylactic treatment for depression is discussed. The effectiveness of lithium has been documented; however, it can have side-effects such as renal lesions. Therefore, indications for lithium treatment should be well defined and well monitored. Thymoleptic agents, such as tricyclic agents, have also been used on a long-term basis. They are preferable to lithium in some cases where difficulty is encountered because of lithium's side-effects or difficulty in maintaining serum lithium levels. However, antidepressants also have side-effects which must be carefully monitored. 16 references.

004373 Itil, T. M.; Soldatos, C. no address **Clinical neurophysiological properties of antidepressants.** In: Hoffmeister, F., Handbook of experimental pharmacology, vol. 55/I. Berlin, West Germany, Springer-Verlag, 1980. (p. 437-469).

The clinical neurophysiological properties of antidepressants are reviewed. Quantitative analysis of scalp recorded EEGs demonstrates that the effects of antidepressants are dose and time related. The majority of classic antidepressants produces thymoleptic EEG reactions. These EEG alterations are characterized by an increase of very slow and very fast activities and a decrease of alpha-waves in the primary wave measurements of the computer analysis, and a decrease of slow and an increase of fast activities in the first derivative measurements. Compounds producing these changes are tricyclic antidepressants. Some antidepressants produce effects similar to those seen after psychostimulant compounds. These changes are characterized by an increase of alpha and slow beta-activities, and a decrease of slower and faster potentials in the primary wave measurements. The third group of compounds, some of them neuroleptics, produce slow-waves and some superimposed fast activities in EEG. The systematic changes in human EEG within a few hours of oral administration of a single dose of antidepressants suggest a specific type of biochemical alteration, probably in the reticular activating system of the brainstem. 90 references.

004374 Janowsky, David S.; Davis, John M. University of California, San Diego, CA 92037 **Cholinergic mechanisms in mania and depression: questions of specificity.** In: Belmaker, R., Mania: an evolving concept. Jamaica, NY, SP Medical and Scientific Books, 1980. 403 p.

The possible role of cholinergic factors in the regulation of affective disorders is reviewed and implications of research findings to the question of whether or not mania is a specific disease or a nonspecific cluster of symptoms are discussed. Studies using cholinesterase inhibitors, investigations of the effects of physostigmine and neostigmine, research on the mood depressant effects of physostigmine and the depressant effects of acetylcholine precursors, studies on the rebound effects in manics following physostigmine administration, and research on the antagonistic effects of methylphenidate and physostigmine and on the cholinergic and anticholinergic effects of psychotropic drugs are seen as indicating that shifting central adrenergic/cholinergic balance regulates affect in man. No support for a role for acetycholine in affect regulation was noted. Specificity studies in manic-depressives versus normals and affect disordered patients in general, as well as in mania versus schizophrenia, suggest that homeostatic mechanisms in the CNS of the manic-depressive patient may be faulty, and that an imbalance of adrenergic and cholinergic factors could explain the excessive activation and inhibition in these patients. They also suggest that mania and schizophrenia are symptom complexes that pharmacologically respond similarly, at least to adrenergic and cholinergic agents. 37 references.

004375 Kabes, J.; Dostal, T.; Nahunek, K.; Svestka, J.; Molcan, J.; Caplova, T.; Hynek, K.; Faltus, F.; Holland, R. P. C. Institute of Psychiatry, Praha, Czechoslovakia **Multicentre study with viloxazine (Vivalan) in depressed patients.** International Pharmacopsychiatry. 15(4):228-239, 1980.

The efficacy and side-effects of viloxazine (Vivalan) at doses of 100 to 300mg daily for 1 month were evaluated in 115 inpatients with moderate to severe depressive illness (including endogenous, involutional, and neurotic depression). Multicenter data for the 106 patients completing the trial indicate statistically significant improvement, as measured by the Hamilton Rating Scale, from day 3 of treatment onwards. Although many of these Ss had previously proven resistant to antidepressive treatment, the average response rate was 71%. Global assessment, similarly indicated early improvement, and 86% of the patients were considered improved by the end of the study period. Side-effects, primarily gastric disturbance, were generally mild and transient and did not prevent continuation of treatment. 13 references. (Author abstract modified)

004376 Kielholz, P.; Kelly, D.; Adams, C. Psychiatrischen Universitatsklinik, Wilhelm-Klein-Strasse 27, CH-4025 Basle, Switzerland **Guidelines on the diagnosis and treatment of depression.** In: Kielholz, P., The general practitioner and his depressed patients. Bern, Switzerland, Hans Huber, 1981. 142 p. (p. 123-133).

Guidelines for the general practitioner on the diagnosis and treatment of depression are presented. Diagnosis depends on obtaining a detailed history and conducting a thorough physical examination. Both the basic and accessory symptoms of the depressive syndrome are summarized. Characteristics of somatogenic depressions and endogenous depressions are cited. The use of pharmacotherapy in the treatment of depression is discussed. Specific aspects considered are selection of the appropriate antidepressant, the dosage and duration of antidepressive medication, parenteral treatment with antidepressants, and additional medication.

004377 Kline, N.; Sacks, W. no address **Treatment of depression with an MAO inhibitor followed by 5-HTP – an unfinished research project.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):233-241, 1980.

An unfinished study of the treatment of depression with a monoamine oxidase (MAO) inhibitor followed by 5-hydroxytryptophan (5-HTP) is described. Fifty nine patients with symptoms of depression were selected, regardless of whether depression was or was not the primary diagnosis. All patients were placed on an MAO inhibitor a minimum of 3 days before the 5-HTP injection. Over half of the patients showed at least some response within 24 hours to either 25mg or 50mg of 5-HTP. Upon more prolonged treatment in a conventional manner, the 14 patients showing no change and the six patients with partial improvement eventually responded favorably. A panel discussion of these results is appended. 27 references.

004378 Kolata, Gina Bari. no address **Clinical trial of psychotherapies is under way.** Science. 212(4493):432-433, 1981.

A National Institute of Mental Health multiinstitutional, clinical trial comparing drugs to two forms of psychotherapy in the treatment of depression is considered. The study is designed to develop a new understanding of psychotherapy by showing how and why it helps depressed people, if it does. Twenty seven therapists have been in training to participate in the study by learning a drug treatment regimen using imipramine, a tricyclic antidepressant, or a placebo, and cognitive behavioral therapy and interpersonal therapy. A total of 144 patients whose depression has been carefully documented will be randomly assigned to one of these four treatments. In addition, 35 patients will be assigned to a treatment as usual group, or referral to experienced therapists who will treat them as they treat their other depressed patients. The efficacy of the therapies will be determined by asking the patients and therapists whether the therapy relieved the patients' symptoms of depression and by conducting an independent clinical evaluation.

004379 Kulkarni, M. R.; Mulay, V. P. B. J. Medical College, Pune 411 001, India **Value of propanidid in electro convulsive therapy (comparison with thiopentone).** Indian Journal of Psychiatry. 22(4):371-374, 1980.

The role of propanidid in ECT was examined and compared with that of thiopentone in 40 patients suffering from psychotic disorders. Propanidid proved to have all the advantages of thiopentone and none of its disadvantages. Its short duration of action suits the short procedure of ECT. It is concluded that the use of propanidid will allow more ECTs to be given in outpatient departments and will help in reducing the patient load on the hospital staff. 7 references.

004380 Lange, Ehrig; Riedel, Christa; Konig, Liesbeth; Liefke, Tilo; Kursawe, Hubertus. Neurologisch-Psychiatrische Klinik, Medizinischen Akademie Democratic Republic **A comparative clinical trial with the tranquilizer trazodone and the tricyclic antidepressant clomipramine.** Klinische Vergleichsprufung Trazodone-Clomipramin. Psychiatrie, Neurologie und Medizinische Psychologie. 32(12):748-750, 1980.

Trazodone and clomipramine were compared for their antidepressant effects and side-effects. Forty patients in two East German cites were given between 200mg and 600mg of either drug over a 2 year period. The findings were evaluated with the Hamilton Depression Scale and the Zerssen Mood Scale. Trazodone was found to have no harmful side-effects, even in combination with other medications, including sedatives. Its primary effect is tranquilizing and anxiolytic, rather than mood improving or activity stimulating. However, clomipramine is more effective for endoreactive and neurotic depression as well as for intravenous treatment of severe depression. Although among nontricyclic antidepressants maprotiline is preferred to trazodone, trazodone's tremor inhibiting qualities in alcoholics warrant further study.

004381 Lideman, R. R.; Panteleyeva, G. P.; Tsutsul'kovskaya, M. Ya.; Vartanyan, F. Ye.; Belyayev, B. S. Institut psikhiatrii AMN SSSR, Moskva, USSR **/The effect of naloxone on the condition of patients with endogenous psychoses./** Vliyaniye naloksona na sostoyaniye bol'nykh endogennymi psikhozami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(2):231-237, 1980.

The effect of naloxone (0.3mg/kg) on the intensity of hallucinations and manic disorders was studied in eight patients one with manic-depressive psychosis and seven with continuous and attack-like schizophrenia) using the double-blind control method. Results indicate the possibility that the endogenous ligands of opiate receptors play a role in the pathogenesis of endogenous mental illnesses, especially those which involve affective and schizoaffective psychoses. Results also show that the reactions of the Ss to naloxone were heterogeneous. These results suggest that further studies should be based on the selection of patients who are sensitive to naloxone. 13 references. (Journal abstract modified)

004382 Loeb, C.; Roccatagliata, G.; Albano, C.; Abbruzzese, G. Clinica Neurologica, Universita di Genova, Via A. De Toni, 5, I-16132 Genova, Italy **/Cerebrospinal fluid values of HVA and 5-HIAA in patients with endogenous depression during the course of treatment./** Valori liquorali di HVA e 5-HIAA in pazienti affetti da depressione endogena in corso di trattamento. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie. 126(1):27-32, 1980.

Homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) were determined in the lumbar cerebrospinal fluid of 17 patients affected by endogenous depression. The modifications of the amine metabolites after treatment (tricyclics, bromocriptine, trazodone, electroconvulsive therapy) were not related to the specific therapy nor to the clinical improvement. In 11 patients, HVA and 5-HIAA showed opposite modifications. The possible role of interactions between dopaminergic and serotonergic systems in the pathogenesis of endogenous depression is discussed. 16 references. (Journal abstract)

004383 Mann, J. John; Friedman, Eitan; Georgotas, Anastase; Gershon, Samuel. Dept. of Psychiatry, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 **The antidepressant effects of trazodone and inhibition of platelet serotonin reuptake.** Communications in Psychopharmacology. 4(4):293-301, 1980.

Trazodone was demonstrated to produce rapid in vivo inhibition of platelet serotonin reuptake in patients suffering from endogenous depression. This effect did not show significant correlation with clinical response, which took several days to occur. No significant direct correlation could be demonstrated between clinical response and reuptake inhibition although responders showed significantly greater serotonin reuptake inhibition than nonresponders, without a significant difference in trazodone plasma levels. It is suggested that if serotonin reuptake inhibition is related to the antidepressant action of trazodone, then it may be via secondary effects that take time to develop. 23 references. (Author abstract)

004384 Meco, Giuseppe; Casacchia, Massimo; Tardi, Marina; Aniello, Raffaele. 1. Clinical Neurologica, Universita di Roma, Roma, Italy **/Activity of bromazepam and lorazepam in neurotic depressions./** Ativita del bromazepam e del lorazepam nelle depressioni nevrotiche. Rivista di Psichiatria. 15(6):566-573, 1980.

Forty neurotic outpatients with depression, anxiety, and somatic symptoms were treated with 4.5mg to 18mg/day bromazepam or 2.5mg to 15mg/day lorazepam for 2 to 8 weeks (mean 4.6 weeks) in a double-blind randomized study. Assessment was based on the Hamilton Rating Scale for Depression. The clinical parameters were consistently improved by both drugs. Although bromazepam was slightly more effective in cases of depression, and lorazepam was slightly more effective in cases of anxiety, the difference in response to both drugs was negligible. It is concluded that benzodiazepines alone are suitable for patients suffering from depression and anxiety of neurotic origin. Results of various antidepressant studies are reviewed. 24 references. (Journal abstract modified)

004385 Montgomery, S. A.; Tiplady, B. Dept. of Academic Psychiatry, St. Mary's Hospital, Harrow Road, London, England **Single dose pharmacokinetic data on zimelidine in depressed patients.** Neuropharmacology. 19(12):1221-1222, 1980.

The single dose pharmacokinetics of zimelidine in depressed patients are described. The liquid chromatographic method of Westerlund, Nilsson, and Jaksch (1979) was used for determination of plasma levels of zimelidine and norzimelidine in 19 depressed patients. Results show that the pharmacokinetic profile in this group of depressed patients did not differ greatly from that seen in healthy volunteers. However, there appears to be a tendency for the half-lives to be longer and more variable in the patient group. Low intersubject variability of norzimelidine levels is noted. 6 references.

004386 Murphy, J. E.; Ankier, S. I. Clinical Research International Ltd., 435/437, Wellingborough Road, Northampton NN1 4EZ, England **An evaluation of trazodone in the treatment of depression.** Neuropharmacology. 19(12):1217-1218, 1980.

Two studies of the clinical efficacy in depression and tolerance for trazodone, a new antidepressant drug, are described. Both studies were double-blind group comparison, in which patients between 18 and 65 years presenting with a primary diagnosis of depression, with or without anxiety, were investigated. The duration of treatment was 8 weeks in the comparison with amitriptyline (n=112) and 4 weeks in the comparison with doxepin (n=101). Results show that the efficacy of trazodone with these general practice patients is comparable to both amitriptyline and doxepine, while side-effects are generally mild and transient.

004387 Nakanishi, K.; Hinoki, M.; Baron, J. B. Hinoki: Dept. of Otolaryngology, Faculty of Medicine, Kyoto University Sakyo Ku, Kyoto, Japan **/Studies on the treatment and diagnosis of neurotic vertigo from the viewpoint of neurootology: observation of balance test for analyzing neurotic vertigo."/** Etudes sur le traitement et le diagnostic des vertiges nevrotiques du point de vue de la neuro-otologie: observation sur les vertiges nevrotiques." Agressologie. 21(3):155-164, 1980.

The balance test for analyzing neurotic vertigo was used in 54 Ss, and the effects of cloxazolam in treating neurotic vertigo were studied. The Ss were mostly neurotic, although there were a few cases of epilepsy and depression. The Ss were given several standard balance tests as well as the balance test, which was created by the authors for analyzing neurotic vertigo. Results show that type-A ataxia exists in a large proportion of Ss with traumatic neurosis, but not in Ss with neurosis or depression. Cloxazolam was given to the Ss in doses of 3 to 6mg/day; depressed Ss also received amitriptyline. Results show that cloxazolam is useful in reducing vertigo in Ss with type-A ataxia, but is not very useful in treating neurotic Ss. In depressed patients cloxazolam did not give good results, but amitriptyline often did prove to be beneficial. 8 references.

004388 Okuma, Teruo; Inanaga, Kazutoyo; Otsuki, Saburo; Sarai, Keisuke; Takahashi, Ryo; Hazama, Hidefumi; Mori, Atsuyoshi; Watanabe, Shosuke. Dept. of Psychiatry, Tohoku University School of Medicine, 1-1, Seiryo-machi, Sendai, Japan **A preliminary double-blind study on the efficacy of carbamazepine in prophylaxis of manic-depressive illness.** Psychopharmacology. 73(1):95-96, 1981.

A preliminary double-blind controlled study on the prophylactic effect of carbamazepine on 22 recurrent manic-depressive psychotics using an inert placebo in 10 Ss is described. Carbamazepine in the dosage of 200 to 600mg was administered for 1 year. Among the 22 carbamazepine Ss, carbamazepine was found to be effective in 60% of cases, and inert placebo was found effective in 22% of cases. It is suggested that carbamazepine is a useful drug for the prophylaxis of manic-depressive illness. 6 references. (Author abstract)

004389 Ostroumova, L. I. Kafedra psikhiatrii, Kubanskiy meditsinskiy institut im. Krasnoy Armii, Krasnodar, USSR **/The nosological independence of involutional depression and its dynamics during psychopharmacotherapy./** K voprosu o nozologicheskom obosoblenii involyutsionnykh depressiy i osobennostyakh ikh dinamiki pri psikhofarmakoterapii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(9):1361-1366, 1979.

The nosological status of involutional depressions and the effects of psychopharmacotherapy on depression were studied in clinical and followup examinations of 92 patients (89 women and 3 men). A control group of 17 patients with late onset endogenous psychoses (schizophrenia) also was examined. During the study the Ss received various psychopharmacological substances, mostly combinations of antidepressants (imipramine or amitriptyline) with tranquilizers (including chlordiazepoxide) and neuroleptics. Results show that the systematic use of psychopharmacotherapy gradually reduces the severity of productive psychopathological disorders, and sometimes reduces depression to a neurosis-like level. 23 references.

004390 Panteleyeva, G. P.; Mikhaylova, N. M.; Belyayev, B. S. Vtoroye klinicheskoye otdeleniye, Institut psikhiatrii, AMN SSSR, Moskva, USSR **/Comparative characteristics of the prophylactic properties of short-term and long-acting lithium carbonate preparations in endogenous affective psychoses./** Sravnitel'naya kharakteristika profilakticheskikh svoystv karbonata litiya kratkovremennogo i retardirovannogo deystviya pri endogennykh affektivnykh psikhozakh. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(3):412-420, 1981.

Comparative characteristics of the prophylactic properties of short-term and long-acting lithium carbonate preparations in endogenous affective psychoses were studied in 53 patients (20 to 60 years old) with manic-depressive psychosis and schizophrenia. The duration of the disease in most of the Ss was 5 to 15 years. A group of 35 patients was examined in two stages. Results show that long-acting lithium carbonate preparations have an advantage over short-term preparations in preventing relapses of affective and schizoaffective psychoses because of their regular and even absorbability in the tissue. This affects both the quantitative and qualitative characteristics of the course of the disease. 21 references. (Journal abstract modified)

004391 Peselow, Eric D.; Dunner, David L.; Fieve, Ronald R.; Lautin, Andrew. 1322 East 84th Street, Brooklyn, NY 11236 **Prophylactic effect of lithium against depression in cyclothymic patients: a life-table analysis.** Comprehensive Psychiatry. 22(3):257-264, 1981.

A life table analysis was used to examine the prophylactic effect of lithium in the treatment of depression in a followup study of 64 bipolar or cyclothymic patients. Ss were studied until the occurrence of one of three outcomes: termination well, failure, or dropout. Of the 64 patients, 22 were followed for 2 years on lithium alone. Results reveal that lithium's effectiveness in preventing depressive episodes in cylcothymics seems less than with other affective subgroups when one measures the time to one depressive episode. There was a 35.2% to 47.3% probability of cyclothymics remaining free of a depressive episode after 1 year. The 50% probability of these patients remaining free of depressive episodes on lithium ranged from 8 to 11.54 months. The need for further study of the benefits of lithium maintenance therapy in cyclothymic patients is noted. 21 references.

004392 Petrie, W. M.; McEvoy, J. P.; Wilson, W. H.; Ban, T. A.; Guy, W. Tennessee Neuropsychiatric Institute, Clinical Research Service, Vanderbilt University, 1501 Murfreesboro Rd., Nashville, TN 37213 **Viloxazine in the treatment of depressive neurosis: a placebo and standard (imipramine) controlled clinical study.** International Pharmacopsychiatry. 15(3):193-196, 1980.

The therapeutics effect of viloxazine hydrochloride, a bicyclic drug with a pharmacologic profile similar to tricyclic antidepressants, were compared to those of imipramine or placebo in a 4 week double-blind trial with 33 depressive neurotic patients. Significant improvement was observed in all treatment groups. Imipramine exhibited significant improvement earlier in depressive symptoms, while viloxazine showed significant improvement earlier in anxious symptoms. The same frequency of treatment emergent symptoms occurred in the treatment groups. Premature termination as a consequence of adverse reactions was required in only one viloxazine and one placebo patient. 7 references. (Author abstract modified)

004393 Pickar, David; Lake, C. Raymond; Cohen, Robert M.; Jimerson, David C.; Murphy, Dennis L. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Alterations in noradrenergic function during clorgyline treatment.** Communications in Psychopharmacology. 4(5):379-386, 1980.

The effect of 4 weeks of treatment with the selective monoamine oxidase (MAO) type-A inhibitor, clorgyline, on noradrenergic function was assessed in depressed patients using steady-state intravenous tyramine pressor response tests and determinations of plasma norepinephrine (NE). During the pretreatment period: 1) the resting levels of plasma NE were correlated with tyramine sensitivity; 2) significant increases in plasma NE accompanied a steady-state rise in blood pressure; and 3) the magnitude of tyramine stimulated NE increases were highly correlated with pretreatment plasma NE levels. Clorgyline administration for 3 to 4 weeks was accompanied by: 1) large increases in pressor sensitivity to intravenous tyramine; 2) significant decreases in resting levels of plasma NE; 3) alterations in the relationship between plasma NE and tyramine sensitivity; and 4) a trend toward a reduction in the tyramine stimulated plasma NE release. A postulated clorgyline induced down regulation of presynaptic adrenergic activity is discussed with regard to the overall enhancement in tyramine pressor sensitivity produced by clorgyline. 33 references. (Author abstract modified)

004394 Pierce, D. Psychiatric Clinic, East Glamorgan Hospital, Church Village, Pontypridd, Mid Glamorgan, Wales **A comparison of trazodone and dothiepin in depression.** Neuropharmacology. 19(12):1219-1220, 1980.

The efficacy of trazodone, a novel antidepressant drug, and dothiepin were compared for the long-term treatment of depressive illness. Forty one male and female patients between the ages of 20 to 65 years who had not suffered symptoms of depression for longer than 18 months received trazodone or dothiepin for 24 weeks. Patients were assessed at 1, 2, 4, 12, and 24 weeks using the Beck self-rating depression scale, a global rating of clinical state, Hamilton Depression Scale, and notation of any significant side-effects. Trazodone was equally effective as dothiepin, and appeared to have a more rapid onset of action.

004395 Pinder, R. M.; Blum, A.; Stulemeijer, S. M.; Barres, M.; Molczadzki, M.; Rigaud, A.; Charbaut, J.; Israel, L.; Kammerer, T. Organon International BV, Scientific Development Group, PO Box 20, 5340 BH Oss, The Netherlands **A double-blind multicentre trial comparing the efficacy and side-effects of mianserin and chlorimipramine in depressed in- and outpatients.** International Pharmacopsychiatry. 15(4):218-227, 1980.

Mianserin (60 mg daily) was compared to chlorimipramine (150mg daily) in the treatment of 145 depressed inpatients and outpatients in four centers. The trial was double-blind and fully randomized. Both drugs were effective antidepressants. No significant differences in efficacy could be demonstrated by means of the Hamilton Rating Scale for Depression, the Beck self-rating scale, or the clinical global impression, for both inpatients and outpatients. Hypotension, dry mouth, and tremor increased significantly more in outpatients after treatment with mianserin. No differences were found between the drugs for other side-effects. 13 references. (Author abstract)

004396 Poldinger, W.; Reinhardt, B. Kantonale Psychiatrische Klinik, CH-9500 Wil/St. Gallen, Switzerland **Neurotropic drugs as co-medication to psychotropics: combined administration of a neurotropic drug and a tetracyclic antidepressant.** International Pharmacopsychiatry. 15(3):137-142, 1980.

Interactions of EMD 21 657, an neurotropic drug used in the treatment of organic brain syndrome, and maprotiline were studied in 40 depressive outpatients. All Ss received daily doses of maprotiline; half also received EMD 21 657 during an initial treatment of 10 days. Ss receiving both drugs reported a faster onset of antidepressant action than controls; this earlier improvement was statistically significant for the target symptom obsessive rumination. Experimental Ss also showed less side-effects than controls, but the difference was not significant. 6 references. (Author abstract modified)

004397 Polimanti, S. Ospedale Civile A. Murri, Fermo (Ascoli Piceno), Italy **/Clinical results obtained with the use of Lysoneuro in depressive syndromes./** Risultati clinici ottenuti con l'impiego di lysoneuro nelle sindromi depressive. Rivista di Neuropsichiatria e Scienze Affini. 26(3):189-211, 1980.

The effects of Lysoneuro were studied in a double-blind controlled clinical trial. Sixty patients, half of them with the depressive neurotic syndrome and half of them with other depressive syndromes of varying severity and pathologic patterns, were given either Lysoneuro or a placebo in a balanced ratio. Patients were evaluated by psychiatric interview and by administration of the Middlesex Hospital Questionnaire. After day 30 of treatment, patients were categorized as cured, improved, or not improved. Lysoneuro proved effective in the depressive neurotic syndrome without other pharmacologic treatment. In the most severe depressions, such as the endogenous and endoreactive depressions, Lysoneuro proved a valuable adjutant to the basic pharmacological treatment. It is concluded that Lysoneuro is effective as a natural thymoleptic agent. 7 references. (Journal abstract modified)

004398 Post, Robert M.; Bunney, William E., Jr. Section on Psychobiology, Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Progress in psychopharmacology.** Current Psychiatric Therapies. 19:69-87, 1980.

Data concerning the clinical subtypes of depressed patients who tend to respond better to antidepressant treatments and the preliminary efforts that have been made using biochemical markers (norepinephrine, serotonin, and dopamine) are reviewed. Attention also is directed to techniques for monitoring the adequacy of blood levels for lithium, neuroleptics, tricyclics, and monoamine oxidase inhibitors; possible modes of action of ECT; the responses of patients with recurrent affective episodes to treatment with either the tricyclic antidepressants or with lithium carbonate; the neuroleptics and dopaminergic mechanisms in the acute psychoses; dopamine receptor agonists in mania, schizophrenia, and Parkinson's disease; the action of carbamazepine as a temporal lobe/limbic anticonvulsant in affective illness; drug combination approaches; and polypeptide and endocrine approaches. 79 references.

004399 Ramseier, F.; Gastpar, M.; Girard, J. Gastpar: Psych. Univ. Klinik, Wilhelm Klein-Strasse 27, CH-4025 Basel, Switzerland **TSH, HGH, HPr, and cortisol response to TRH in depressed patients.** Acta Psychiatrica Belgica. 80(4):399-409, 1980.

Intravenous and oral stimulation with thyrotropin releasing hormone (TRH) in depressed patients was studied. Thyroid stimulating hormone (TSH), human growth hormone (HGH), prolactin (HPr), cortisol, triiodothyronine (T3), T4, and RT4 were measured in patients after an overnight fast, after injection of .2mg TRH, after 40mg oral administration of TRH and after 3 weeks of antidepressant treatment. Results seem to indicate that only endogenous depression shows a deficiency in pituitary response to TRH, and they confirm some previously established hormonal patterns such as low TSH response, no growth hormone (GH) stimulation, and normal prolactin. After antidepressant treatment more normal patterns emerged. It also appears that there is an earlier response to oral stimulation than to intravenous stimulation. 29 references. (Journal abstract modified)

004400 Rickels, Karl; Case, W. George; Diamond, Lenore. 203 Piersol Building, Hospital of the University of Pennsylvania, 3400 Spruce St., Philadelphia, PA 19104 **Relapse after short-term drug therapy in neurotic outpatients.** International Pharmacopsychiatry. 15(3):186-192, 1980.

A 6 month followup was carried out on 184 anxious and depressed neurotic outpatients who had reported improvement after controlled drug trials of several weeks duration. An astonishing relapse rate of 81% for anxious and 87% for depressed patients was found. Early as compared to late relapse was associated with more chronicity and less improvement at the end of the drug trials, while type of drug received did not affect relapse. Onset of relapse had no effect on help-seeking behavior. At the time of followup, nonrelapsed patients had lowest and untreated relapsed patients had highest symptom levels. It is concluded that short-term drug treatment alone does not represent sufficient therapy for chronic neurotic anxious or depressed outpatients. 10 references. (Author abstract)

004401 Rounsaville, Bruce J.; Klerman, Gerald L.; Weissman, Myrna M. Substance Abuse Treatment Unit, Connecticut Mental Health Center, 100 Park St., New Haven, CT 06511 **Do psychotherapy and pharmacotherapy for depression conflict? Empirical evidence from a clinical trial. (Unpublished paper).** Research Report, NIMH Grant R01-MH-26466, 1979. 31 p.

Six hypotheses about negative interactions between pharmacotherapy and psychotherapy were evaluated based on data derived from a clinical trial of psychotherapy and tricyclic antidepressants alone and in combination as treatment for 91 ambulatory depressives. Hypotheses regarding the negative effects of pharmacotherapy on psychotherapy include: 1) the negative placebo effect; 2) the view that drug-induced reduction of symptoms reduces the motive for continuing psychotherapy; 3) the view that pharmacotherapy undercuts psychological defenses; and 4) proposed deleterious effects of pharmacotherapy on psychotherapy expectations. The hypotheses relating to possible negative effects of psychotherapy on pharmacotherapy include the view that psychotherapy may be symptomatically disruptive, and a proposed biochemical replacement effect of drugs. None of the hypotheses were confirmed by a study of the process, outcome, and posttreatment behavior of depressed patients, and it is concluded that the combination of treatments is more effective than either treatment is alone. 15 references. (Author abstract modified)

004402 Rowan, P.; Paykel, E. S.; Parker, R. R.; West, E. Dept. of Psychiatry, St. George's Hospital Medical School, London SW17, England **Comparative effects of phenelzine and amitriptyline: a placebo controlled trial.** Neuropharmacology. 19(12):1223-1225, 1980.

Results of a double-blind comparison of phenelzine, amitriptyline, and a placebo in outpatient neurotic depressive Ss are reported. Data from the 131 patients completing the 6 week study indicate that both drugs showed significant effects at 2, 4, and 6 weeks. The two drugs appear to have closely similar effects (which are primarily antidepressant) on the core symptoms of depressed mood. Phenelzine may also have some weak antianxiety effects, although similarities are more striking than differences. 13 references.

004403 Rubin, Robert T.; Poland, Russell E.; Blodgett, A. L. Nelson; Winston, Robert A.; Forster, Bella; Carroll, Bernard J. Dept. of Psychiatry, Harbor-Univeristy of California at Los Angeles Medical Center, Torrance, CA 90509 **Cortisol dynamics and dexamethasone pharmacokinetics in primary endogenous depression: preliminary findings.** Research Report, NIMH Grant 5P01-MH-28380, 1980. 12 p.

Aspects of cortisol secretory dynamics in depression are discussed, including nocturnal hypersecretion, escape from dexamethasone suppression, and urinary free cortisol levels, and these hormone parameters are related to the severity of depressive symptomatology. The various cortisol parameters were correlated in the 15 patients with their Hamilton and Beck total depression scores. The correlations were of a low order, suggesting that there is no apparent relationship between the degree of cortisol secretory hyperactivity and the severity of depressive symptomatology. 18 references.

004404 Rybakowski, Janusz; Chlopocka-Wozniak, Maria; Kapelski, Zdzislaw. Katedra i Klinika Psychiatrii AM, ul. Szpitalna 27/33, 60-572 Poznan, Poland /**Clinical evaluation of the prophylactic effectiveness of prolonged lithium carbonate therapy in endogenous depressive syndromes.**/ Ocena kliniczna skutecznosci profilaktycznej dlugotrwalego stosowania weglanu litu u chorych z endogennymi zespolami depresyjnymi. Psychiatria Polska. 14(4):357-361, 1980.

The quantitative prophylactic effect of lithium carbonate was evaluated in 61 patients with bipolar affective illness who had been receiving lithium for a period of 1 to 8 years. The course of the illness and the number of hospitalizations in the periods prior to and during lithium therapy were compared for each patient. It was found that the overall number of recurrent phases and the number of psychiatric hospitalizations had decreased during lithium administration by 71% and 72%, respectively. A complete prophylactic effect (absence of morbid symptoms during lithium administration) was obtained in 44% of the patients, and a partial effect (decrease in the number of relapses by more than 50%), in 28% of the patients. It was also found that the prophylactic effect obtained in patients who had been on lithium for 1 to 3 years did not differ essentially from the effect obtained in those who had been receiving lithium for 4 to 8 years. 17 references. (Journal abstract modified)

004405 Sachar, Edward J.; Halbreich, Uriel; Asnis, Gregory; Nathan, R. Swami; Halpern, Frieda S. New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032 **Neuroendocrine disturbance in depression.** In: Brambilla, F., ed., Progress in psychoneuroendocrinology. New York, Elsevier/North Holland, 1980. 669 p. (p. 263-272).

Plasma cortisol samples were obtained every half hour over 24 hours in 24 unmedicated, hospitalized, endogenously depressed patients. Half of the patients were cortisol hypersecretors with flattened circadian cortisol patterns; the other 12 showed normal cortisol secretory patterns. Most of the hypersecretors were over 50 years of age. The 2mg dexamethasone test was positive in 6 of the 24 patients, 5 of which were hypersecretors; however, more than half of the hypersecretors were undetected by the dexamethasone test. Cortisol hypersecretion appeared to be responsible for the relative insulin resistance seen in 8 of 16 patients, but was not associated with the blunted thyroid stimulating hormone responses to thyrotophin releasing hormone noted in 11 of 21 patients. Dextroamphetamine (0.1mg/kg i.v.) rapidly suppressed cortisol to normal levels in depressed Ss, but it elicited cortisol release in healthy control Ss. Results suggest abnormal noradrenergic regulation of cortisol secretion in endogenous depressives. 11 references.

004406 Schatzberg, Alan F.; Orsulak, Paul J.; Rosenbaum, Alan H.; Maruta, Toshihiko; Kruger, Ellen R.; Cole, Jonathan O.; Schildkraut, Joseph J. Affective Disease Program, McLean Hospital, 115 Mill Street, Belmont, MA 02178 **Toward a biochemical classification of depressive disorders IV: pretreatment urinary MHPG levels as predictors of antidepressant response to imipramine.** Communications in Psychopharmacology. 4(5):441-445, 1980.

The hypothesis that patients with low pretreatment urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) levels respond more favorably to treatment with imipramine than do patients with high MHPG levels was evaluated in a prospective study of 24 patients with major depressive disorders. A favorable response to treatment with imipramine was observed at 4 weeks in a significantly larger proportion of patients with pretreatment urinary MHPG levels lower than 1950 mcg/24 hours than in patients with MHPG levels greater than 1950 mcg/24 hours. Thus, these results support the notion that measurement of pretreatment urinary MHPG levels may provide a useful clinical laboratory test for assessing the likelihood of favorable response to imipramine. 21 references. (Author abstract modified)

004407 Schlienger, J. L.; Kapfer, M. Th.; Singer, L.; Stephan, F. Serv. d'Endocrinologie et des Maladies de la Nutrition, Pavillon Leriche, Cent. Hospitalier Universitaire, F-67.005 Strasbourg Cedex, France /**Different effects of tricyclic and tetracyclic antidepressants on the release of TSH, prolactin, and growth hormone after administration of thyrostimulating releasing hormone in manic-depressives.**/ Effets differents d'antidepresseurs tricycliques (clomipramine et amitriptyline) et tetracyclique (maprotiline) sur la reponse de thyrostimuline, de prolactine et d'hormone somatotrope apres thyroliberine chez des patients atteints de psychose. Acta Psychiatrica Belgica. 80(5):584-599, 1980.

The hormonal alterations induced by tricyclic and tetracylic antidepressants were studied in patients with manic-depressive psychosis to ascertain the role of certain biogenic amines in the regulation of thyroid stimulating hormone (TSH), prolactin (PRL), and growth hormone (GH). The responsiveness of plasma TSH, PRL, and GH to synthetic thyrostimulating release hormone (TRH) was determined in 57 patients distributed in five groups according to treatment: 10 nontreated patients, 16 tricyclic (clomipramine and amitriptyline) treated patients, 6 patients treated with clomipramine in association with lithium, 6 tetracyclic (maprotiline) treated patients, and 19 patients treated with major neuroleptics. Basal plasma levels of TSH were normal in all patients. The TSH response to TRH (delta TSH) was blunted in nontreated patients. Delta TSH was normal in the patients treated with maprotiline or neuroleptics and increased in the group treated with tricyclic antidepressants in association with lithium. Basal plasma levels of PRL and PRL response to TRH (delta PRL) were decreased in women treated with tricyclic antidepressants, but remained normal using maprotiline. They were markedly increased in the neuroleptic group. No inadequate response of GH to TRH was noted. Results are discussed in terms of actions of antidepressants on brain monoamines. 25 references. (Author abstract modified)

004408 Schou, Mogens. no address **Lithium treatment of manic-depressive illness. A practical guide.** Basel, S. Karger, 1980. 72 p. $14.50.

A practical guide to the management of manic-depressive illness with lithium salts is presented. A concise account is given of the main background information on affective illness and its treatment with lithium. A description of the features of manic-depressive illness and its treatment, the development of lithium therapy, practical management, undesirable effects, a prospective look at lithium, and do's and don'ts of lithium therapy are covered. A glossary is included.

004409 Sheard, M. H.; Marini, J. L. Yale University School of Medicine, New Haven, CT 06510 **Lithium and aggressive behavior.** In: Gershon, S., Lithium: controversies and unresolved issues. Amsterdam, Excerpta Medica, 1979. (p. 136-147).

A review of human clinical studies which indicates that lithium can inhibit overt aggressive behavior and calm angry affect is presented. The clinical characteristics of the lithium responsive S are delineated. A brief overview of possible mechanisms of action for lithium's antiaggressive effect suggests that toxic, placebo, motor, or sensory reaction time effects of lithium do not influence gross motor coordination. More research is indicated on endocrine effects and the possible genetic connections between manic-depressive illness, sociopathy, and hysterical character disorders. 32 references. (Author abstract)

004410 Ulrich, G. Abteilung fur Psychophysiologie, Freie Universitat Berlin, Nussbaumallee 32-38, D-1 Berlin 19, West Germany **/On the relationship between measures obtained by video analysis of nonverbal behavior and self-rating of mood./** Uber den Zusammenhang videoanalytisch gewonnener Masse des non-verbalen Verhaltens mit selbst eingeschatzter Befindlichkeit. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie. 125(2):349-359, 1979.

The condition of 13 manic-depressive patients was assessed during a symptom free interval while under treatment with lithium and again after a 6 week placebo period. A behavioral analysis of videotaped interviews and a self-rating of mood were examined. Significant relationships were found between the relative duration of speech activity and the relative frequency of hand movements accompanying speech. Speech activity and hand movement parameters were related significantly to the mood dimensions of social affect and relation. It is noted that conventional scales have low sensitivity for the course evaluation of depression, while the behavioral procedure is sensitive even in the subclinical range. In addition, the behavioral procedure has a theoretical impact on the fundamental question of the physiological basis of manic-depressive illness. 22 references. (Journal abstract modified)

004411 Veith, Richard C.; Friedel, Robert O.; Bloom, Valerie; Bielski, Robert. Gerontology Research, Education and Clinical Center, V.A. Medical Center, GRECC 182 B, Seattle, WA 98108 **Electrocardiogram changes and plasma desipramine levels during treatment of depression.** Clinical Pharmacology and Therapeutics. 27(6):796-802, 1980.

Twenty six symptomatic Ss who met Research Diagnostic Criteria for major affective disorder and were free of cardiovascular disease were treated for 3 weeks with a fixed dosage schedule of desipramine (DMI) to a maximum of 200mg/day. An electrocardiogram (ECG) and DMI plasma level determinations were obtained before treatment and weekly thereafter. DMI levels during the trial ranged from 13.4 to 882.2ng/ml. DMI treatment was associated with increase in heartrate (p less than .001), prolongation of the PR (p less than .001), QRS (p less than ,001), and QTc intervals (p less than .001), and increase in T-wave amplitutde (p less than .001). Significant (p less than .001), but relatively weak, correlations were noted between DMI plasma levels and heartrate (r=.405), QRS interval (r=.346), QTc interval (r=.534), and T-wave amplitude (r=-.386). PR interval prolongation was independent of DMI levels (r=.171). DMI treatment induced no clinically significant ECG alterations or cardiovascular adverse effects. The relevance of DMI plasma level and the possible roles of other contributing factors in the production of these ECG changes are discussed. 28 references. (Author abstract)

004412 Walinder, J.; Carlsson, A.; Persson, R.; Wallin, L. no address **Potentiation of the effect of antidepressant drugs by tryptophan.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):243-249, 1980.

Potentiation of the effects of a bicyclic antidepressant drug, zimelidine, by concurrent administration of tryptophan was investigated in 24 patients suffering from endogenous depression. The combination of tryptophan with zimelidine did not enhance the antidepressive effect of zimelidine, as measured by rating scales of depressive/anxiety symptoms. The lack of potentiating effects of tryptophan might be explained by the fact that zimelidine is such a potent serotonin reuptake inhibitor that additional tryptophan does not mean any substantial increase in transmitter concentration at receptor sites. A panel discussion of these findings is appended. 8 references.

004413 Weissman, Myrna M. Depression Research Unit, Connecticut Mental Health Center, 904 Howard Ave., Suite 2A, New Haven, CT 06519 **Pharmacotherapy and psychotherapy for ambulatory depression: efficacy and choices.** Research Report, NIMH Grant 5R01-MH-26466, 1980. 25 p.

Research on the drugs and psychotherapy for treating depressed outpatients is reviewed, and an attempt is made to translate the evidence into clinical terms to guide the choice of treatment. It is suggested that the motivation for clinical trials of psychotherapy among ambulatory depressed patients is derived from three sources: epidemiology, economics of reimbursement, and the ethics of providing safe and effective care. Five therapies which have been used widely in treating depression (cognitive therapy, interpersonal psychotherapy, behavior therapy, marital therapy, and group therapy) are examined. Evidence for the efficacy of the five psychotherapies alone, in comparison, and in combination with drugs for the ambulatory depressed patient is summarized. It is concluded that the combined treatment approach generally is favored, but that there is great variability in patient and clinician preferences. Findings from research on the symptoms, social functioning, and diagnostic subtypes of depressed patients are reviewed to help guide the clinician's selection of an effective treatment. The need for multicenter collaborative trials to test the efficacy of several therapeutic conditions with and without drugs in large population samples is emphasized. 13 references.

004414 Wheatley, David. General Practitioner Research Group, Twickenham, England **Trazodone in depression.** International Pharmacopsychiatry. 15(4):240-246, 1980.

Three trials were conducted to evaluate the efficacy, side-effects, and dosage regimens of trazodone in the treatment of depression with or without anxiety. In the first two trials, dose comparisons were undertaken in 59 patients suffering mixed depression and anxiety with either predominating and 87 patients suffering from predominant depression with or without anxiety. While therapeutic effects were the same for once, twice, and three times daily dosage, once daily dosage produced drowsiness while the thrice daily dosage did not. However, the incidence of dizziness was nonsignificantly higher on the thrice a day regimen, relative to the other two dosage schedules. In the third trial (a double-blind comparison to the tricyclic antidepressant imipramine) antidepressant effects were similar, except at 6 weeks, when imipramine was significantly better than trazodone. There were no significant differences in relief of anxiety symptoms. 6 references. (Author abstract modified)

004415 Woggon, Brigitte. Psychiatrische Universitatsklinik Zurich, Forschungsdirektion, Postfach 68, CH-8029 Zurich, Switzerland **/Changes in psychopathologic symptoms during 20 days of treatment with antidepressants and neuroleptic drugs./**

Veranderungen der psychopathologischen Symptomatik wahrend 20tagiger antidepressiver oder neuroleptischer Behandlung. Psychiatria Clinica. 13(3-4):150-164, 1980.

In a retrospective study, 266 psychiatric patients treated with neuroleptics and 130 patients treated with antidepressants were divided into groups of responders and nonresponders following termination of therapy. The groups were compared with respect to psychopathological symptoms, as assessed by the AMP diagnostic system, on days 0, 5, 10, and 20 posttreatment. Responders and nonresponders showed significant differences in the target syndrome from day 5 onward, and these differences were also noted on day 20. Improvements found at several points of testing, expressed as a percentage of the overall improvement after 20 days, showed that the major part of the total improvement took place during the first 10 days of treatment. The statistically significant changes were examined for practical relevance by giving their declared variance as a proportion of the total variance. 15 references. (Journal abstract modified)

004416 Wysocki, Henryk; Rybakowski, Janusz; Wierusz-Wysocka, Bogna; Kapelski, Zdzislaw; Szajnerman, Zofia. Klinika Hematologii, Inst. Chorob Wewnetrznych, Akademia Medyczna, ul. Szkolna 8/12, 61-833 Poznan, Poland /**An attempt to assess the effect of lithium on the neutrophil leukocyte system in affective psychosis.**/ Proba oceny wplywu litu na uklad granulocytow obojetnochlonnych u chorych z psychozami afektywnymi. Psychiatria Polska. 14(4):363-367, 1980.

The neutrophil leukocyte system was examined in eight patients with affective psychosis prior to and 10 days after lithium carbonate therapy. The number of neutrophils in the peripheral blood was determined; a hydrocortisone test of the bone marrow reserve and an adrenaline test of the marginal pool were conducted. In all cases the number of neutrophils in the peripheral blood was found to have increased under the influence of lithium. In six cases a distinct increase in the reserve pools also was found, while the marginal pool was unmistakably reduced in all subjects. The obtained results show that the mechanism of action exerted by lithium on the neutrophil leukocyte system is more complex than has been thought to date. 6 references. (Journal abstract modified)

004417 Zaccara, G.; Ferrara, M.; Ardito, P. Clinica delle malattie nervose e mentali, Universita degli Studi di Firenze, Firenze, Italy /**Controlled clinical trial of nomifensine in the treatment of depression.**/ Studio clinico controllato della nomifensina nella terapia degli stati depressivi. Rivista di Patologia nervosa e mentale. C(3):111-120, 1979/80.

The therapeutic efficacy of nomifensine and nortriptyline was evaluated in a double-blind study of 29 patients suffering from various kinds of depression. The results of the first 15 days of treatment are discussed. The drugs were administered on a flexible dosage schedule, from 50 to 125mg/day in two to three separate doses. Hamilton's Depression Scale was administered before treatment and again on days 5, 10, and 15 of the study. Based on scores from Hamilton's Depression Scale and other measures the antidepressant effect of nomifensine was judged comparable to that of nortriptyline. No significant differences were noted in its range of action. No side-effects were detected in the dosages administered. 19 references. (Journal abstract modified)

004418 Zuckerman, Diana M.; Prusoff, Brigitte A.; Weissman, Myrna M.; Padian, Nancy S. Depression Research Unit, Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06520 **Personality as a predictor of psychotherapy and pharmacotherapy outcome for depressed outpatients. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-26466, 1979.

Depressed outpatients were randomly assigned to one of four treatment groups (psychotherapy, pharmacotherapy, combined psychotherapy and pharmacotherapy, and nonscheduled treatment) in a double-blind, randomized clinical trial of personality as a predictor of outcome. Before treatment, Ss were assessed on three personality inventories (the Maudsley Personality Inventory, Frank's Mastery Scale, and the Buss-Durkee Guilt Scale) and four outcome scales (Hamilton Depression Scale, Raskin Depression Scale, Global Illness Scale, and Social Adjustment Self-Report). The Ss were reassessed on the outcome measures at termination (after 2 to 16 weeks of treatment) and 1 year later. The pretreatment personality scores were not significantly related to improved outcome scores at termination, either as a main effect or for the interaction with treatment group. However, low neuroticism and high extroversion on the Maudsley Inventory were associated with improved social adjustment 1 year later. Implications for theories and treatment of depression are discussed. 22 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

004419 Bertoletti, P. Ospedale S. Maria della Pieta, Roma, Italy /**Prazepam: a new benzodiazepine for the treatment of anxious-depressive states.**/ Prazepam: un nuovo benzodiazepinico nel trattamento degli stati ansioso-depressivi. Rivista di Neuropsichiatria e Scienze Affini 26(3):135-138, 1980.

Twenty anxious-depressive patients characterized by neuroticism were treated with 20 to 90mg/day of prazepam for a period of 10 to 45 days. Changes over the course of treatment were rated by means of the Wechsler scale. Approximately 80% of the patients showed improvement in the first 2 weeks of treatment. Prazepam was well tolerated, and no treatment was suspended due to adverse reactions. Renal, heart, and liver functions were unimpaired, and blood values were not adversely affected. Prazepam is judged to be as efficacious as the other benzodiazepines for the treatment of depression and has the advantage of producing fewer side-effects. 5 references. (Journal abstract modified)

004420 Downing, Robert W.; Rickels, Karl. Psychopharmacology Research and Treatment Unit, Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **Responders and nonresponders to chlordiazepoxide and placebo. A discriminant function analysis. (Unpublished paper).** Final Report, NIMH Grant 5R01-MH-31366, 1980. 11 p.

Data were obtained from 356 anxious outpatients treated with either chlordiazepoxide or placebo in 4 week long, double-blind drug trials and were analyzed to determine predictors of treatment response using extreme groups and discriminant function analysis. Symptom severity was assessed in terms of the scores from five factors (somatization, obsessive-compulsive, interpersonal sensitivity, depression, and anxiety). According to the Hopkins Symptom Checklist, chlordiazepoxide response was greater in younger female patients with lower levels of initial depression and a more favorable prognosis. Placebo response was greater in younger, Black, previously untreated patients, favorably drug treated patients, and in patients with lower initial somatization and depression. Discriminators that were found between drug and placebo response include age, previous drug treatment, race, and initial level of somatic symptomatology. 10 references. (Author abstract modified)

004421 Garzya, Giovanni. Div. Geriatrica, Ospedale Generale V. Fazzi, Lecce, Italy /**Clinical use of a new benzodiazepine, prazepam.**/ Impiego clinico di un nuovo benzodiazepinico, il prazepam. Lavoro Neuropsichiatrico. 66(3):27-31, 1980.

Thirty five patients (25 women and 10 men between ages 55 and 70), diagnosed as anxious and/or depressive, were treated with average doses of 20mg prazepam for 25 days. Symptoms improved after 2 weeks of treatment. Side-effects were negligible. Tables summarize the patients and their mental states prior to treatment, as well as the effects of prazepam. 6 references. (Journal abstract modified)

004422 Itoh, Hitoshi; Takahashi, Ryo; Miura, Sadanori. Dept. of Neuropsychiatry, Keio University, 35 Shinanomachi, Shinjukuku, Tokyo, Japan **Alprazolam, a new type anxiolytic in neurotic patients: a pilot study.** International Pharmacopsychiatry. 15(6):344-349, 1980.

The efficacy, safety, and optimal dosage of alprazolam, a new triazolobenzodiazepine anxiolytic agent, were investigated. Ss were 115 neurotic patients, who were treated with alprazolam for 4 weeks in an open label study The daily dose ranged from 0.4mg to 3.2mg, with an average of 1.4mg. A slight to remarkable improvement was experienced by 73% of Ss, and a particularly high improvement rate was observed in patients with initially severe sleep disturbances. No serious side-effects were noted. A comparison of the characteristics of insomniac and noninsomniac neurotic patients suggests that neurosis with insomnia might represent an acute or aggravated phase of the disease. The validity of the new Psychoneurotic Rating Scale, in comparison with the Hamilton Anxiety Rating Scale, is discussed. 11 references. (Author abstract modified)

004423 Johnstone, Eve C.; Bourne, Rachel C.; Crow, T. J.; Frith, C. D.; Gamble, S.; Lofthouse, R.; Owen, F.; Owens, D. G. C.; Robinson, J. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England **The relationships between clinical response, psychophysiological variables and plasma levels of amitriptyline and diazepam in neurotic outpatients.** Psychopharmacology. 72(3):233-240, 1981.

Substantial clinical improvement was observed in neurotic outpatients treated for 4 weeks with amitriptyline, diazepam, amitriptyline and diazepam, or placebo. No clear relationships among clinical change, psychophysiological change, and plasma drug levels were observed. There was no relationship found between plasma drug levels and cigarette smoking. It is concluded that neither the plasma levels of amitriptyline and diazepam nor changes in skin conductance responsivity offer a useful guide to the clinical response to drug treatment. 34 references. (Author abstract modified)

004424 Liebowitz, Michael R.; Klein, Donald F. Dept. of Psychiatry, College of Physicians and Surgeons, Columbia University, 722 West 168th St., New York, NY 10032 **Differential diagnosis and treatment of panic attacks and phobic states.** Annual Review of Medicine: Selected Topics in the Clinical Sciences. 32:583-599, 1981.

Recent developments in the differential diagnosis, pathophysiology, pharmacotherapy, and behavioral treatment of severe anxiety (panic) attacks and various phobic states are reviewed. A case of agoraphobia is presented in detail to illustrate clinical issues and to serve as a basis for discussing differential diagnosis. The presence or absence of spontaneous panic attacks has crucial implications for classifying phobic states. Data and speculations concerning the pathophysiology of agoraphobia, social phobia, and simple phobia are also presented. Systematic densensitization, flooding, and exposure in vivo are discussed. 46 references. (Author abstract modified)

004425 Mavissakalian, Matig; Barlow, David H. University of Pittsburgh School of Medicine, Pittsburgh, PA **Phobia: psychological and pharmacological treatment.** New York, Guilford, 1981. 256 p.

The literature on psychological and pharmacological treatment of phobias is reviewed with specific reference to current asessment procedures and therapy programs for specific phobias and agoraphobia. Treatments, which are among the most frequently used behavioral and cognitive behavioral therapies for the treatments of specific phobias, are detailed: ungraded in vivo exposure; graded in vivo exposure methods (participant modeling and reinforced practice); imagery based exposure methods (systematic desensitization and imaginal flooding); and cognitive behavioral treatment strategies (self-statement training). A case study illustrates how a recommended treatment program can be a combination of several treatment modalities. Future directions in the assessment and treatment of phobias are discussed: 1) research on the basis mechanisms of fear; 2) research on the mechanisms of action or active ingredients inherent in currently successful treatments; 3) research on refining existing procedures in the treatment of a variety of fears, particularly the delivery of these techniques; and 4) investigation of the use of pharmacological agents, most likely in combination with various psychotherapeutic interventions. 81 references.

004426 Olajossy, Marcin; Modrzewska, Romana. Klinika Psychiatrii AM, Abramowicka 2, 20-442 Lublin, Poland **/An evaluation of the usefulness of the acylase test in neuroleptic treatment./** Ocena przydatnosci stosowania testu acylazowego przy kuracjach neuroleptycznych. Psychiatria Polska. 14(5):471-474, 1980.

The activity of cobalt activated acylase was determined in 48 patients receiving neuroleptic treatment. Its value had been O i.u. before treatment in all patients. In the second week of treatment low values were found in eight patients despite maximum drug doses. In the fourth week of treatment the values of acylase increased despite considerable diminution of doses and exceeded 1 i.u. in 22 of the patients examined. The mean values of acylase activity did not differ significantly after 4 weeks of treatment in patients treated for the first time and in those who had been treated repeatedly. 8 references. (Journal abstract modified)

004427 Rifkin, Arthur; Klein, Donald F.; Dillon, Donald; Levitt, Morton. Dept. of Psychiatry, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY 10029 **Blockade by imipramine or desipramine of panic induced by sodium lactate.** American Journal of Psychiatry. 138(5):676-677, 1981.

The effect of sodium lactate infusions on a group of nine Ss with panic disorder and on nine controls was investigated to test hypotheses that: 1) sodium lactate would cause panic in the experimental Ss and not in controls; and 2) tricyclic antidepressants (imipramine or desipramine) would prevent panic attacks during a second sodium lactate infusion in the six Ss whose spontaneous attack stopped during prior treatment with these drugs. The findings confirmed these hypotheses although caution is suggested in light of the preliminary nature of the study. 7 references.

004428 Scharbach, H. 9, rue de Gigant, F-44000 Nantes, France **/A double-blind trial: the use of oxprenolol and diazepam in anxiety./** Essai en double aveugle (oxprenolol/diazepam) dans l'anxiete. Encephale. 7(1):51-58, 1981.

The effectiveness of oxprenolol vs. diazepam in treating anxiety was studied in a double-blind experiment. Thirty six Ss suffering from somatic and/or psychological anxiety were given either 80mg of oxprenolol (19 Ss) or 5mg of diazepam (17 Ss) in 1 tablet daily at the beginning of the study. This dosage was increased to an average of three tablets daily. Effectiveness was measured on the basis of the Hamilton scale for anxiety and by the subjective evaluations of patient and physician. Results show equally good results on the basis of the subjective evaluations; statistically, however, oxprenolol is more effective than diazepam in treating anxiety. 12 references

004429 Semke, V. Ya. Kafedra psikhiatrii, Altayskiy meditsinskiy institut, Barnaul, USSR **/Possibilities of pathogenetic therapy of hysteria./** O vozmozhnostyakh patogeneticheskoy terapii isterii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(3):420-425, 1981.

Possibilities of pathogenetic therapy of hysteria were studied in 371 patients with hysteria and 180 patients with hysteriform disturbances. The Ss were examined clinicodynamically and neurophysiologically to determine the necessity for pathogenetic treatment in relation to the stage and degree of the emotional disturbances. In cases of an acute or subacute course of the disease, combinations of hypnosuggestive therapy with modified autogenic training were effective. For patients with a lingering course, combinations of psychotherapeutic and biological methods with the use of central cholinolytics (for relaxing the high tone of the cholinergic system), and psychostimulants and antidepressants (for strengthening the tone of the serotoninergic structures) were effective. In resistant cases, medicinal therapy with medium and high doses of atropine was effective. Results show that an individualized, staged complex approach to the treatment of hysteria which considers the age factor is the most effective. 21 references. (Journal abstract)

004430 Snyder, Scott. Dept. of Psychiatry, Baylor College of Medicine, Texas Medical Center, Houston, TX 77030 **The interaction of psychopharmacology and psychoanalysis in the borderline patient.** Psychiatric Quarterly. 52(4):240-250, 1980.

The interrelationships between the psychoanalytic and psychopharmacological perspectives are explored as they aid in unifying the concept and definition of the borderline personality. The major psychoanalytic conceptualizations of the borderline personality are reviewed, as is the use of medication response as an aid to diagnosis of the borderline. Four borderline subtypes are delineated, with a focus on the central role of affect in this disorder and implications for psychopharmacological treatment. The four subtypes include: 1) a group characterized by impulsive and negative behavior and hostile depression characterized by a reversal of vegetation signs; 2) a group of patients manifesting erratic behavior, marked by rebellion and overt anger, alternating with depression; 3) an affectless group, marked by extreme obsessional and schizoid styles; and 4) a group showing a clinging depression with diminished self-esteem and high anxiety (including panic attacks). Analogous diagnostic classifications of these groups (e.g., hysteroid dysphoric, emotionally unstable character disorder) are noted, and drug response of these groups is reviewed. It is suggested that analysis of medication response may aid in better delineating the syndrome. 51 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

004431 Agnoli, A.; Ruggieri, S.; Falaschi, P.; Mearelli, S.; Del Roscio, S.; D'Urso, R.; Frajese, G. Clinica Neurologica, University of L'Aquila, I-67100 L'Aquila, Italy **Are the enkephalins involved in Parkinson's disease? Clinical and neuroendocrine responses to naloxone administration.** Advances in Biochemical Psychopharmacology. 22:511-521, 1980.

Clinical and neuroendocrine responses to naloxone administration were studied in parkinsonism patients, and research concerning the possible involvement of the enkephalins in Parkinson's disease is reviewed. Results indicate that 2mg of naloxone induces an inconsistent improvement in tremor, rigidity, and in the Webster Rating Scale score while bradikinesia shows a tendency to worsen. Moreover, these results are present only briefly (2 to 3 hours). However, the dosage of 8mg induces a constant improvement in the three symptoms, tremor in particular. Also, the overall clinical picture (Webster Rating Scale score) was much improved. Naloxone did not modify plasma prolactin levels in either of the two dosages. These data show that parkinsonism is not only a consequence of damage in the nigrostriatal system, but a consequence of alterations in the entire dopamine system. 34 references.

004432 Allen, Marcia Divoll; Greenblatt, David J.; Harmatz, Jerold S.; Shader, Richard I. Greenblatt: Division of Clinical Pharmacology, Box 1007, New England Medical Center, 171 Harrison Ave., Boston, MA 02111 **Desmethyldiazepam kinetics in the elderly after oral prazepam.** Clinical Pharmacology and Therapeutics. 28(2):196-202, 1980.

Desmethyldiazepam (DMDZ) kinetics were investigated in 15 young (22 to 42 years old) and 14 elderly (62 to 85 years old) Ss, administered single oral doses of 20mg prazepam. Plasma DMDZ concentrations were determined in venous blood samples drawn up to 9 days after the dose. Appearance in blood of DMDZ was slow, with peak plasma levels reached in an average of 10 to 20 hours. First-order DMDZ appearance was observed in only 17 Ss. Volume of distribution of total DMDZ (range, 1.33 to 6.31/kg) and of unbound DMDZ after correction for protein binding (range, 43 to 243l/kg) was larger in women than in men of all ages, and in the elderly as opposed to the young. Elimination half-life (range, 29 to 224 hours) rose with age in men (r=.66, p less than .01), but not in women (r=.02). Clearance of unbound DMDZ (range, 2.9 to 31.2ml/min/kg) was greater in women than in men of all ages, and declined with age in men (r=.40), but not in women (r=.06). As in the case of diazepam, age can influence DMDZ kinetics, but changes in drug disposition with age may differ between the sexes. 20 references. (Author abstract modified)

004433 Avrutskiy, G. Ya.; Laskova, N. B. Otdel psikhofarmakologii, Moskovskiy NII psikhiatrii Ministerstva zdravookhraneniya RSFSR, Moskva, USSR **/Some principles of differentiated metabolic drug treatment in comprehensive therapy of mental disorders./** Nekotoryye printsipy differentsirovannogo primeneniya preparatov metabolicheskoy terapii v kompleksnom lechenii psikhicheskikh zabolevaniy. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(8):1077-1083, 1979.

A study of 246 patients with schizophrenia, manic-depressive psychoses, and psychoorganic syndrome who were all treated with metabolic action drugs (piracetam, piriditol, and pantogam) elucidated the efficacy of these preparations in a comprehensive treatment of mental disorders. The desirability or necessity of including these drugs in a pharmacotherapy program is discussed in the light of clinical trials. During such trials, certain aspects of the clinical effects with each drug were examined, permitting a comparison of the pharmacological activity of piracetam, piriditol, and pantogam. It is recommended that these drugs be used only after careful evaluation of the mental state of the patient and the clinical profile of the drug. 29 references. (Journal abstract modified)

004434 Balakleyevskiy, A. I.; Mimyukova, T. A.; Vashenin, M. M.; Gayduk, F. M. Problemnaya lab. biokhimii neyrogormonov i regulyatsii obmena veshchestv, Minskiy meditsinskiy institut, Minsk, USSR **/Correction of the extrapyramidal neuroleptic syndrome by tryptophan and the time course of its content in the blood of patients./** Korrektsiya ekstrapiramidnogo neyrolepticheskogo sindroma triptofanom i dinamika yego soderzhaniya v krovi bol'nykh. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(2):95-97, 1981.

Correction of the extrapyramidal neuroleptic syndrome by tryptophan and the time course of its content in the blood were studied in 44 patients of both sexes (20 to 55 years old) with various forms of the syndrome, and in a control group of eight healthy people of both sexes (22 to 40 years old). The patients were divided into three groups according to the form of the syndrome affecting them. Group 1 consisted of 15 Ss with moderately severe akinetic hypertonic disorders; group 2 consisted of 21 Ss with chronic hyperkinetic hypertonic disorders; and group 3 consisted of eight Ss with chronic hyperkinetic disorders. Following the development of extrapyramidal syndrome the Ss were given 0.6g of tryptophan by mouth. The behavioral condition of the Ss was measured before and after the administration of tryptophan, and the tryptophan content of the blood was measured using the Yudenfrend method. Results show that tryptophan brought about an improvement in 73% of the patients in group 1, 52% of group 2, and 37% of group 3. 19 references. (Journal abstract modified)

004435 Benkert, O. Psychiatrische Klinik der Universitat Munchen, Nussbaumstrasse 7, D-8000, Munchen 2, West Germany **Pharmacotherapy of sexual impotence in the male.** Modern Problems of Pharmacopsychiatry. 15:158-173, 1980.

Drugs which have been prescribed in instances of sexual impotence in the male or whose effectiveness has been observed or experimentally tested are described. The substances fall into the following categories: 1) hormones (androgens, luteinizing hormone, releasing hormone, thyroid hormone, and thyrotropin releasing hormone); 2) drugs influencing biogenic amines (L-dopa, apomorphine, bromocriptine, PCPA, parachloromethylamphetamine, methysergide, and danitracen); 3) vasodilators (nitrites, oxytocin, and yohimbine); 4) psychopharmacological drugs (neuroleptics, antidepressants, lithium salts, tranquilizers); and 5) other psychotropoic drugs, such as aphrodisiacs. It is concluded that no pharmacotherapy for organically healthy patients with sexual impotence has been experimentally substantiated, and that physicians should avoid prescribing drugs for problems observed in their patients. Instead focus should be on organic causes, behavioral changes due to physiological aging, open communication between physician and patient, and psychotherapy and behavior therapy. 62 references.

004436 Boszormenyi, Zoltan. National Institute for Nervous and Mental Diseases, Mandula u. 36, H-1025, Budapest, Hungary **Pharmacological influence of sexual functions in adolescents.** Modern Problems of Pharmacopsychiatry. 15:131-144, 1980.

The occurrence of sexual dysfunction in adolescence is addressed and the influence of drug treatments on such disorders is discussed. It is contended that these syndromes are often related to primary endocrine or developmental defects, but that they also result from purely educational or psychological and emotional problems. Adolescents often have difficulty in seeking help, and psychotherapy in combination with anxiolytic agents as an adjunct to treatment is seen as being helpful. Benzodiazepines have proven especially effective. Since teenagers are dependent on the expectations of parents, it is suggested that administration of drugs should be fully understood by the involved family members. It is argued that the adolescent has less anxiety tolerance, fewer emotional brakes, less facility for elaborating symptoms or symbolic levels, and diminished capacities for postponement of impulsive gratifications, and that all of these factors are important in achieving effective results in combined psychotherapy and pharmacotherapy. 12 references.

004437 Breuning, Stephen E.; Ferguson, Donald G.; Cullari, Salvatore. Psychological and Research Services, Coldwater Regional Center for Developmental Disabilities, Coldwater, MI 49036 **Analysis of single-double blind procedures, maintenance of placebo effects, and drug-induced dyskinesia with mentally retarded persons.** Applied Research in Mental Retardation. 1(3/4):175-192, 1980.

The importance of reliability checks, placebo conditions, and double-blind conditions in assessing medication effects with 10 institutionalized mentally retarded Ss was examined. A procedure for discontinuing the use of placebo and double-blind conditions was explored, and all Ss received weekly assessments and 1 year followup of withdrawal and persistent dyskinesia. The results empirically demonstrate the importance of using reliability checks, placebo conditions, and double-blind conditions. The procedure for discontinuing placebo and double-blind conditions was effective, and is discussed in terms of ethical and practical issues concerning their use in institutions. Place effects were observed to last 12 or more weeks and are discussed in terms of being maintained via operant variables. Withdrawal dyskinesias were present in 9 of the 10 Ss and a 1.5 year followup showed persistent dyskinesias in 6 of the 10 Ss. Lip-mouth and tongue movements were the primary dyskinesias. 14 references. (Author abstract modified)

004438 Breuning, Stephen E.; O'Neill, Michael J.; Ferguson, Donald G. Psychological and Research Services, Coldwater Regional Center for Developmental Disabilities, Coldwater, MI 49036 **Comparison of psychotropic drug, response cost, and psychotropic drug plus response cost procedures for controlling institutionalized mentally retarded persons.** Applied Research in Mental Retardation. 1(3/4):253-268, 1980.

The effectiveness of psychotropic drugs, response cost, and psychotropic drug plus response cost procedures in controlling the inappropriate behaviors of 18 institutionalized mentally retarded Ss is discussed. Ss were randomly assigned to one of two sequences. Sequence 1 utilized 11 Ss and was drug, drug plus response cost, then response cost. Sequence 2 utilized seven Ss and was drug, placebo (no drug), the response cost. Ss and staff were blind to conditions and sequences. The results show that the frequencies of inappropriate behaviors were lowest during the response cost conditions. The drug, drug plus response, and placebo conditions resulted in similar frequencies of inappropriate behaviors. These frequencies were about 45% higher than those obtained during the response cost conditions. Withdrawal dyskinesias and symptoms were present in 13 of the 18 Ss, and a 1 year followup showed persistent dyskinesias present in 7 of the 18 Ss. Results are discussed in terms of drug/behavior interactions and legal and programmatic implications for habilitative training with mentally retarded persons. 19 references. (Author abstract modified)

004439 Cazzullo, C. L.; Altamura, A. C.; Cornaggia, C. M.; Canger, R.; Pruneri, C. Altamura: Depto. di Psichiatria Clinica, Universita di Milano, Padiglione Guardia II, Policlinico di Milano, I-20100 Milano, Italy **Therapeutic plasma levels of some anticonvulsants in focal epilepsy in relation to computerized axial tomography.** Encephale. 7(2):191-197, 1981.

Antiepileptic drug blood levels needed to control seizures were studied in 37 patients with established focal epilepsy. The patients examined by computerized axial tomography (CAT) were grouped according to whether they did or did not show evidence of an organic focal lesion in the brain. Statistical elaboration of the data revealed that CAT positive patients required significantly higher mean antiepileptic drug blood levels for clinical effectiveness than did CAT negative patients. Single drugs failed to produce control at any plasma level, necessitating recourse to multidrug regimes significantly more often in the CAT positive than in the CAT negative patient group. Possible reasons for the observed differences of therapeutic responses are discussed. 16 references. (Journal abstract modified)

004440 Chinaglia, L. Divisione Neurologica, Ospedale Civile Carretta, Montebelluna, Italy /**Pharmacokinetic study in man of the CH-757 preparation.**/ Studio farmacocinetico nell'uomo del preparato CH 757. Revista de Neuropsichiatria e Scienze Affini. 26(2):55-60, 1980.

The characteristics of the bioavailabilty of CH-757 (lormetazepam) in humans were studied. Eight patients between ages 40 and 63 who had been hospitalized with neurological disorders were selected. All patients received 5mg lormetazepam. Blood was drawn before and at 2, 4, 6, and 12 hours after treatment. Lormetazepam levels in blood and urine were monitored. Although the pharmacological effects lasted only 4 to 5 hours, the level of plasmatic CH-757 remained elevated for 8 to 12 hours. Seventy one percent of the drug was excreted in the urine within 72 hours. Lormetazepam is in large part transformed into a composite in the blood. It is presumed that urinary metabolism is also in large part composed of this composite. 2 references. (Journal abstract modified)

004441 Danner, Rolf. Dept. of Clinical Neurophysiology, Central University Hospital Kuopio, SF-70210 Kuopio 21, Finland / **Measurements of nerve conduction velocity during decreasing toxic diphenylhydantoin levels and the beginning of carbamazepine medication: a clinical neurophysiological report.**/ Messungen der Nervenleitgeschwindigkeit beim Abklingen einer Diphenylhydantoinintoxikation und wahrend des Beginns einer Carbamazepinmedikation: eine klinisch-neurophysiologische Dokumentation. Archiv fur Psychiatrie und Nervenkrankheiten. 229(3):267-272, 1981.

A clinical neurophysical report of an epileptic patient recovering from acute diphenylhydantoin toxicity is presented. Sensory and motor nerve conduction velocity was determined daily and at the beginning of administration of the anticonvulsant drug carbamazephine. A statistical correction which accounts for the influence of variable skin temperatures on the sensory nerve conduction velocity proved to be useful for measuring sural nerves. A significant correlation was found between the increasing sensory nerve conduction of the spinal nerves and the decreasing diphenylhydantoin levels. Decreasing conduction velocities in peripheral nerves during rising carbamazepine concentrations were observed. 22 references. (Journal abstract modified)

004442 Davis, Kenneth L.; Hollister, Leo E.; Stahl, Steven M.; Berger, Philip A. Hollister: Stanford University, Stanford, CA 94305 **Cholinomimetics in Huntington's disease.** Research Report, NIMH Grant MH-30854, 1980 5 p.

The use of physostigmine salicylate and choline chloride with Huntington's disease patients was investigated. Patients were administered intravenous propantheline bromide until the heartrate reached 100, at which time they were administered 4.0mg intravenous physostigmine. Choline chloride was administered gradually over 4 weeks for a maximum dose of 20gm per day in four divided doses, and within subject comparisons of choline chloride versus placebo periods were undertaken. Physiological and videotape monitoring indicated that physostigmine produced a significant decrease in choreic movements 30 minutes after the termination of the infusion in 9 of 10 patients. Of the nine patients who completed 12 weeks of choline chloride testing, seven had a significant decrease in their choreic movement frequencies. It is suggested that physostigmine and choline chloride increase brain acetylcholine activity by different mechanisms. It is concluded that although increasing brain acetylcholine activity is a potential treatment strategy for the choreic movements of Huntington's disease, neither physostigmine nor choline chloride can be considered a practical clinical treatment for the disease, since more potent cholinomimetics may be needed to more consistently reduce choreic movements. 7 references.

004443 Deisenhammer, E.; Sommer, R. Institut fur Klinische Neurophysiologie, Medizinisches Laboratorium, Wagner-Jauregg-Krankenhaus, Linz, Austria /**Serum concentration of anticonvulsants. Pharmacokinetic findings and their practical application.**/ Die Serumkonzentration der Antikonvulsiva. Pharmakokinetische Erkenntnisse und deren praktische Anwendung. Wiener Klinische Wochenschrift. 91:571-578, 1979.

The regular determination of serum concentrations of anticonvulsants and their contribution to pharmacokinesis are discussed. The measurement of serum concentrations makes possible the determination of actually available unbound, and therefore effective substances. It is indicated that the metabolism of these anticonvulsants varies, and the relationship between a given dosage and serum concentration suggests strong individual fluctuation. Through a variety of biological. changes, illnesses, and medication, the body metabolism can be altered, which can lead to a change in the serum concentration of the anticonvulsant. Results of research have shown that a therapeutic concentration area exists which should be taken as a statistical value. Only a specific concentration shows in a certain percentage of patients a reduction of attacks or freedom from attacks. Low concentrations have been used in harmless attacks with sufficient therapeutic effect, while high concentrations have been used in malignant attacks without sufficient effect. It is concluded that this method should be used for all problematical patients. Fifty percent of the patients who had shown no improvement before, showed an improvement or freedom from attacks when this method was used. (Journal abstract modified)

004444 Dement'yeva, N. F.; Yermolina, L. A.; Yezhkova, V. A.; Mozhayeva, Ye. G. no address /**Therapy and social adaptation of oligophrenics (review of the literature).**/ Terapiya i sotsial'naya adaptatsiya bol'nykh oligofreniyey (obzor literatury). Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(3):439-450, 1981.

Therapy and social adaptation of oligophrenics are discussed. Some therapeutic measures are directed towards activating individual mental functions (memory, attention, etc.) and towards pathogenetic treatment. Among the pharmacological substances used in the treatment of undifferentiated mental retardation and minimal brain dysfunction are psychostimulants. The study of these drugs seems to indicate that dopamine is related to this disorder. Neuroleptics help to control the behavior of patients but do not increase their work capacities. Metabolic therapy and biogenic stimulants have also been used with some success in children. Diet therapy and music therapy also have been tried. In connection with the study of the adaptive capabilities of the mentally retarded, studies have been done on interpersonal relations between such people, and between mentally retarded and normal people. It is concluded that the very pathological process of mental retardation is determined to a certain extent by the therapeutic approach to the patient. 136 references.

004445 Deniker, P.; Loo, H.; Zarifian, E.; Peron, P.; Benyacoub, A.; Roux, J. M.; Kamoun, A. Hospital Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France /**A preliminary open study of the use of amineptine of the deficient syndrome of hebephrenics and of addicts during withdrawal.**/ Etude preliminaire en ouvert de l'amineptine sur le syndrome deficitaire des hebephrenes et des toxicomanes au decours du sevrage. Encephale. 7(1):59-64, 1981.

A preliminary study of the effects of amineptine on hebephrenics and addicts was conducted. Nine addicts and 10 hebephrenics received an average of 200mg/day of amineptine. Evaluation was made on the basis of clinical interviews and evaluation scales, self-evaluations, evidence of dependency, and side-effects. Results show improvement in six of the addicts and eight of the hebephrenics. Despite the preliminary nature of this study, it is concluded that amineptine is effective in treating syndromes marked by apragmatism, motor loss, and disinterest. In addition, pre-existing delirious ideas in schizophrenics are not reactivated and there seems to be no risk of drug dependency in addicts. 12 references.

004446 Ducreuzet; Moreau; Pelle. Service de Geriatrie du Centre Hospitalier de Versailles, Versailles, France /**Treatment of psychological and behavioral disturbances in mental deficiency with Duxil.**/ Troubles psycho-comportementaux de l'insuffisance cerebrale: leur traitement par Duxil. Revue de Geriatrie. 6(4):201-204, 1981.

The effectiveness of Duxil in treating mental deficiency in the elderly was studied. Thirty Ss, average age 77, were studied for 2 months. Ss received a placebo during the first month and Duxil during the second month. Ss evaluated themselves on the basis of 17 items which included mental efficiency, neurosensorial equilibrium, and psychoaffective behavior. Results show that after the first month, scores were the same as before treatment. After treatment with Duxil, overall scores improved by 36.5 percent. 1 reference.

004447 Emerson, Ronald; D'Souzas, Bernard J.; Vining, Eileen P.; Holden, Kenton R.; Mellits, E. David; Freeman, John M. Freeman: CMSC 601, Johns Hopkins Hospital, Baltimore, MD 21205 **Stopping medication in children with epilepsy.** New England Journal of Medicine. 304(19):1125-1129, 1981.

Anticonvulsant therapy was discontinued in 68 children with epilepsy who had had no seizures for 4 years, in an attempt to find the risk of relapse and the factors predictive of recurrence. In this population, the probability of remaining free of seizures for 4 years after discontinuation of medication was 69%. Children were more likely to have recurrent seizures if they were mentally retarded, if their seizures had begun before 2 years of age, if they had many generalized seizures before control, or if they had a definitely abnormal EEG before medication was discontinued. Multivariate analysis of variance shows that the best predictors of outcome were the EEG taken at cessation of medication and the number of seizures before control. It is concluded that in the normal child who has not had many seizures and whose EEG is normal or mildly abnormal, the risks of discontinuing medication after 4 seizure free years are acceptable. 13 references. (Author abstract)

004448 Freedman, Daniel X. University of Chicago, Chicago, IL 60637 **LSD, psychotogenic procedures and brain neurohumors. (Unpublished paper).** Final Report, NIMH Grant RO1-MH-13186, 1980. 7 p.

The relationship between psychotogenic procedures and brain amines was investigated with emphasis on the psychopharmacology of indoleamine (especially lysergic acid diethylamide-LSD) and phenylethylamine hallucinogens and their effects of metabolism (binding, synthesis, storage, uptake, release, enzyme activity, compartmentation, and catabolism) of mouse and rat brain amines such as 5-hydroxytryptamine (5-HT), norepinephrine (NE), and dopamine. The experiments demonstrated an effect of LSD on brain 5-HT, LSD concentration and subcellular distribution, turnover of nonpsychotomimetic cogeners such as 2-bromo-LSD, and similar effects of phenylethylamine psychotomimetics on 5-HT concentrations were observed. The effects of stress on 5-HT and NE were demonstrated, as well as the enhancing effect of diminished concentration of 5-HT on the behavioral impact of LSD with reserpine or tetrabenazine pretreatment, after raphe lesions, or PCPA. The correlation of acute behavioral effects in the rat with the half-life of LSD was observed, which was followed by similar demonstration in man. Other findings included the correlation of LSD half-life and amine changes with acute biobehavioral effects and the uniquely high concentration of 5-HT in human pineal and in the blood of autistic and severely retarded children. 2 references.

004449 Gadow, Kenneth D. State University of New York, Stony Brook, NY 11790 **Drug therapy for hyperactivity: treatment procedures in natural settings.** In: Gadow, K., Psychosocial aspects of drug treatment for hyperactivity. Boulder, CO, Westview, 1979. 479 p. (p. 325-378).

Teachers and parents were surveyed to study referral and treatment practices with trainable mentally retarded (TMR) children and adolescents receiving pharmacotherapy for hyperactivity. Teachers completed a questionnaire in which they listed all children in their special education class who received psychotropic drugs during the current year, and described their experience with training in and problems with drug therapy. They then provided detailed information on their involvement in drug therapy. Parents were questioned about the drug regimen, school involvement in medical referral, and physician monitoring procedures. Pharmacotherapy for behavior disorders was relatively common in this sample. Teacher formal training in drug therapy was trivial. School involvement in treatment related procedures was far less than what is advocated by clinicians and researchers, and medical treatment monitoring procedures were not satisfactory. The data are seen as raising questions about the administration and storage of medication in school. 13 references. (Author abstract modified)

004450 Gagne, Pierre. 461 Argyle St., Sherbrooke, Quebec J1J 3H5, Canada **Treatment of sex offenders with medroxyprogesterone acetate.** American Journal of Psychiatry. 138(5):644-646, 1981.

A group of 48 male patients with long-standing histories of deviant sexual behavior received medroxyprogesterone acetate and milieu therapy for up to 12 months. Forty Ss responded positively, all within 3 weeks, with diminished frequency of sexual fantasies and arousal, decreased desire for deviant sexual behavior, increased control over sexual urges, and improvement in psychosocial functioning. Improvement in deviant sexual behavior and psychosocial functioning was maintained after treatment ended, and there was no evidence of permanent physiological changes. It is suggested that medroxyprogesterone acetate associated with counseling may be the treatment of choice for patients with long-term deviant sexual behavior, and the ethical issues involved in this approach are briefly discussed. 6 references. (Author abstract)

004451 Geormaneanu, Mircea; Voiculescu, Viorica. Paedriatic Clinic, 23 August Hospital, Bucharest, Rumania **Treatment of encopresis with imipramine.** Neurologie et Psychiatrie. 18(3):209-210, 1980.

Two case reports of treatment with imipramine of encopresis (involuntary passage of feces unrelated to organic deficit or illness, associated with maternal/child conflict) in 5-year-old and 6-year-old boys are presented. In both cases, imipramine (40 to 50mg/day) promoted rapid sphincter control. It is noted that amoug the commonest adverse effect of imipramine are urinary retention and constipation. It is suggested that these effects are related to the therapeutic action of imipramine in enuresis and encopresis. 1 reference.

004452 Gmur, M.; Uchtenhagen, A. no address /**Methadone treatment of heroin addicts in Switzerland.**/ Die Methadonbehandlung von Heroinabhangigen in der Schweiz. Therapiewoche. 30:1228-1235, 1980.

Methadone treatment combined with other methods of drug (i.e., heroin) treatment in Switzerland is discussed. Methadone is a promising drug when the dangers of misuse and abuse (i.e., involvement in the black market, incorrect diagnosis, and inappropriate treatment) are taken into account. Since deficiencies in stationary treatment for drug addiction are a fact, and ambulatory detoxification treatment has not indicated any notable success, methadone treatment is the recommended alternative. It is concluded that methadone treatment works well when the following guidelines are observed: 1) realistic success expectation, (i.e., drug freedom not the primary goal); 2) conflict free methadone treatment combined with caretaking and therapeutical measures; and 3) long-term treatment. (Journal abstract modified)

004453 Golinko, Barry E.; Rennick, Phillip M.; Lewis, Ronald F. Brookdale Hospital Medical Center, Dept. of Pediatrics, Comp Care Program, 9620 Church Ave., Brooklyn, NY 11212 **Predicting stimulant effectiveness in hyperactive children with a repeatable neuropsychological battery: a preliminary study.** Progress in Neuro-Psychopharmacology. 5(1):65-68, 1981.

The effects of d-amphetamine on performance on the Repeatable Cognitive/Perceptual/Motor neuopsychological test battery (RCPM) were studied in 14 hyperactive children. Results showed that 11 of the children performed better after d-amphetamine. High or low doses of d-amphetamine were effective in 10 of these children, but only the high dose was effective in one child. The use of the RCPM to titrate dosages quickly and to monitor dose effectiveness in long-term followup is discussed. 8 references. (Author abstract modified)

004454 Hechtman, Lily; Weiss, Gabrielle; Perlman, Terrye; Hopkins, Joyce; Wener, Albert. Dept. of Psychiatry, Montreal Children's Hospital, Montreal, Quebec, Canada **Hyperactives as young adults: prospective ten-year followup.** In: Gadow, K., Psychosocial aspects of drug treatment for hyperactivity. Boulder, CO, Westview, 1979. 479 p. (p. 417-442).

A 10 year followup study was conducted on 75 hyperactive Ss (never treated with stimulant drugs) and of 44 normal control Ss between 17 and 24 years old. The findings indicate that while hyperactive Ss continue to have varous difficulties in adjustment, only a small minority show severe psychopathology or serious antisocial behavior. Persisting problems center around continued impulsive traits, low self-esteem, and poor socialization skills. Hyperactive Ss had more court referrals within the 5 years preceding evaluation but were the same as controls within 1 year preceding evaluation. Extent of nonmedical drug use did not differ between groups, and physiological measures were not significantly different. Sequential EEGs of hyperactives taken over 10 years suggest that many readings become normal, and that this normalization takes place mainly in adolescence. A group of 17 Ss who had received chlorpromazine for 18 to 48 months were compared with a matched group of 21 Ss who had received no drug longer than 6 months. No differences were found on any measures of outcome. It is concluded that future treatment programs should focus on social skills, self-esteem, and impulsivity training. 24 references. (Author abstract modified)

004455 Herrmann, W. M.; Beach, R. C. Dept. of Clinical Neuropsychopharmacology, Schering AG, Postfach 650311, D-1000 Berlin 65, West Germany **Pharmacotherapy for sexual offenders: review of the action of antiandrogens with special reference to their psychic effects.** Modern Problems of Pharmacopsychiatry. 15:182-194, 1980.

The effects of pharmacotherapy on the sexual behavior of sexual offenders are examined, with emphasis on the impact of antiandrogen therapy on sexual fantasy, preference, identity, and attitudes, as well as arousability to stimuli mediated by the CNS (e.g., visual stimuli). Six specific aspects of behavior that may be affected by drugs include sexual function, sexual behavior, sexual arousability, gender identity, preferences and attitudes, and sexual gratification. Associated behavioral changes with antiandrogen treatment include depression, a calming down effect (tranquilization), activity, and aggression. Mention is also made of experimental studies with cyproterone acetate. It is concluded that antiandrogen treatment may offer the only possible alternative to castration or lifelong imprisonment in some sex offenders, and that it has particular effects on functional sexuality, inhibition of sexuality, and sexual fantasy. 31 references.

004456 Hoes, M. J. A. J. M.; Colla, P.; Folgering, H. University of Nijmegen, Nijmegen, The Netherlands **Hyperventilation syndrome, treatment with L-tryptophan and pyridoxine; predictive values of xanthurenic acid excretion.** Journal of Orthomolecular Psychiatry. 10(1):7-15, 1981.

A case is made for the pathophysiological importance of the cerebral serotonergic neurons in the hyperventilation syndrome (HVS), whose function depends on the systemic L-tryptophan metabolism. The role of such metabolism was studied in 13 HVS patients via administration of pyridoxine 125mg t.i.d. and L-tryptophan 2g for 4 weeks. The syndrome is caused by stress and common features are increased respiration, anxiety, and occipito-cervical headache and muscular hypertonia. Treatment resulted in freedom from hyperventilation attacks in nine Ss, and extremes of xanthurenic acid excretion, an index of peripheral L-tryptophan metabolism, had disappeared. The findings indicate that the L-tryptophan metabolism is important in the pathophysiology of the HVS and that xanthurenic acid excretion discriminates responders from nonresponders to pyridoxine, L-tryptophan treatment. 42 references. (Author abstract modified)

004457 Hoffet, H. no address /**Clinical application of antiandrogens in psychiatry.**/ Die klinische Anwendung von Antiandrogenen in der Psychiatrie. Gynakologe. 13:33-43, 1980.

The application of antidanrogens, especially cyproterone acetate, to treat sexual deviations of men and resocialization of sexual delinquents is examined. These drugs have been infrequently used for treatment of women with psychosexual disturbances. The effective mechanism of antiandrogens on hormonal, central control of the sexual drive is analyzed thoroughly. Psychiatric effects and side-effects of antiandrogen administration are discussed; problems have surfaced on the medical/ethical level. Today it can be maintained with sufficient certainty that cyproterone acetate does not cause irreversible side-effectsion adult, male patients. If the patient absolutely wants cyproterone acetate, it may be used, but the decision belongs to experienced specialists who are able to take care of the patient psychologically. It is concluded that in intelligent and sensible patients, treatment with antiandrogens results occasionally in a psychic reconstruction. In more primitive patients, resocialization must first be tried through applied psychotherapy. (Journal abstract modified)

004458 Houillon, P.; Kitenge, A.; Jouannigot, R.; Lullien, L. no address /**Some therapeutic effects of Nootropyl.**/ Quelques effets therapeutiques du Nootropyl. Annales Medico-Psychologiques. 138(7):869-876, 1980.

Therapeutic effects of piracetam observed over a 10 year period are discussed. Under certain conditions piracetam acts as a neurotransmitter, and in certain cases it has a GABA-like effect. Cases histories of piracetam's use in cranial trauma, toxic syndromes, cerebral vasculopathies, and epilepsy are discussed. On the basis of these cases it is concluded that: piracetam acts equally on toxic vascular accidents and recent trauma; doses of 10g or more are necessary in cases of possible hypoxia; and best results are obtained in the terminal phases of several presenile dementias. A discussion of the physiological effects of piracetam follows the main article. 13 references.

004459 Indo, Toshikatsu; Ando, Kazuya. Dept. of Neurology, Gifu Prefectural Tajimi Hospital, Maehata-cho 5-161, Tajimi city, 507 Japan **Hyperventilation syndrome and beta receptor function -- clinical effect of beta blocker upon the syndrome.** Japanese Journal of Psychosomatic Medicine. 20(5):424-428, 1980.

In light of the previous observation of an increase in beta-receptor sensitivity and its proposed role in the pathogenesis of the hyperventilation syndrome (HVS), the preventive effects of beta-blocker administration were clinically examined. A daily dosage of 10mg or 15mg of bufetolol hydrochloride was used in 38 cases, while 29 other patients with intense anxiety were administered the same dosage in combination with antianxiety drugs over a period of several months. It was found that: 1) the frequency of attacks decreased significantly with each treatment method; 2) the decrease was more significant in the combination group; and 3) the intensity of attacks significantly decreased under each method, and the decrease was more significant in the combination group. It is concluded that it is necessary to suppress not only the sensitivity of beta-receptors (physical factors), but also anxiety (emotional factors) via the use of antianxiety drugs in the long-term management of hyperventilation syndrome. 11 references. (Journal abstract modified)

004460 Itil, T. M.; Akpinar, S.; Yardim, M.; Dayican, G. Division of Biological Psychiatry, Dept. of Psychiatry, New York Medical College, New York, NY 10029 **Effects of high dosage lisuride hydrogen maleate (LHM) in Parkinson syndrome.** In: Neurochemistry and clinical neurology. New York, Alan R. Liss, 1980.

An open, uncontrolled pilot study was conducted to determine whether high dosage lisuride hydrogen maleate (LHM, daily dosage of 100 to 100mcg with a mean of 462 to 619mcg) has any significant therapeutic effects in 11 patients with Parkinson syndrome treated for a period of 6 weeks. LHM is an isoergolenyl derivative with potent peripheral serotonin antagonist effects in addition to central alpha-adrenergic, antihistaminic, CNS, and central dopaminergic properties. According to the Global Impression rating scale, 8 of the 11 patients showed marked overall improvement, 2 showed moderate improvement, and 1 showed slight improvement. The most significant improvement was established in a variety of symptoms of Parkinson syndrome, as shown by serveral neurological and extrapyramidal symptom scales. The most dramatic improvement was seen in cog wheel rigidity, Parkinson tremor, Parkinson-like gait and posture, and masklike face. Patients also showed an improvement in memory recall and orientation. There were no systematic or noticeable laboratory abnormalities, electrocardiogram deviations, and/or clinical side-effects during LMH treatment.

004461 Izakson, Kh. A. Nevrologicheskoye otdeleniye, Tallinskiy gospital', Tallin, USSR **/The classification of sleep disorders and the treatment of various forms of somnambulism./** Rabochaya gruppirovka narusheniy sna i lecheniye razlichnykh form somnambulizma. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(9):1383-1387, 1979.

The classification of sleep disorders and the treatment of various forms of somnambulism were studied. Sleep disorders were differentiated as follows: sleep without any negative subjective or objective disturbances, predominantly subjective sleep disorders, and predominantly objective motor sleep disturbances (including sleepwalking due to various organic diseases of the CNS, and to neuroses and reactive states). One hundred Ss (16 to 20 years old) suffering from sleepwalking were treated using substances that decreased the duration of slow-wave sleep by increasing the duration of fast-wave sleep at night (proserine during the day and reserpine at night). Also used were chlorpromazine, imipramine, phenobarbital, meprobamate, magnesium sulfate, B-vitamins, chlordiazepoxide, electrosleep, prolonged transcerebral galvanization through the eyes, and physical exercise. Results indicate that a number of these methods have a promising future in the treatment of sleep disorders. 32 references.

004462 Johannessen, Svein. State Epilepsy Hospital, Sandvika, Norway **Aspects of pharmacological effects of antiepileptic drugs.** Acta Neurologica Scandinavica. 62(Suppl. 80):53-55, 1980.

Aspects of drug disposition that may have implications for studies of the pharmacological effects of antiepileptic drugs are briefly reviewed. The importance of measuring serum levels during chronic treatment of epileptic patients is considered and the occurrence of various influences at different stages such as absorption, protein binding, metabolism and excretion is considered. The risks of drug interactions with concomitant changes in drug serum levels are also mentioned.

004463 Jones, Mortyn T.; Gillham, Brian; Beckford, Ursula; Dornhorst, Anne; Abraham, Ralph R.; Seed, Mary; Wynn, Victor. Sherrington School of Physiology, St. Thomas's Hospital Medical School, London SE1 7EH, England **Effect of treatment with sodium valproate and diazepam on plasma corticotropin in Nelson's syndrome.** Lancet. No. 8231:1179-1181, 1981.

The effects of treatment with sodium valproate and diazepam on plasma adrenocorticotropic hormone (ACTH) was investigated in six patients with Nelson's syndrome. Initial high plasma ACTH concentrations were greatly reduced by 3 to 5 weeks' sodium valproate treatment (with and without diazepam). When treatment was stopped, ACTH concentrations returned to their previous levels. Diazepam did not add significantly to the effects of sodium valproate alone. Three patients reported a decrease in the severity and frequency of headaches while on sodium valproate. In five patients, abnormal skin pigmentation was reduced. It is suggested that sodium valproate raises GABA levels in the hypothalamus and that this is responsible for the reduction of ACTH secretion. The data are consistent with the hypothesis that Nelson's syndrome is a neuroendocrine disease caused by a deficiency in the hypothalamic GABAergic system. 13 references. (Author abstract modified)

004464 Kelly, D. Priory Hospital, Priory Lane, London S.W. 15, England **Clinical review of beta-blockers in anxiety.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(5):259-266, 1980.

A clinical review of the use of beta-blockers, such as oxprenolol and propranolol, in treating anxiety is provided. Anxiety consists of: the subjective experience (due to the presence of a situation causing anxiety), avoidance behavior, and autonomic symptoms. Various theories are considered that highlight the psychic and somatic aspects of anxiety. Beta-adrenergic receptor blocking drugs have been used with success in treating everyday stress. The profile of symptoms (such as tachycardia, palpitations, and tremor) which are most likely to respond to beta-blockers are discussed as well as the drug's side-effects. Beta-blockade has been beneficial to patients with the hyperdynamic beta-adrenergic circulatory state, and to those in whom anxiety is associated with autonomic overreaction. The mode of action of beta-blockers is different from that of other anxiolytics, with which they can be combined, and beta-blocking drugs results in a reduction of symptoms, a decrease in pulse rate, and a stabilization of blood pressure and respiration. One of the benefits of beta-adrenergic blockade is that if it can produce symptomatic relief, the subject can as a result lose his anticipatory anxiety without the risk of sedation, habituation, or addiction. 21 references.

004465 Kent, Saul. no address **Assessing L-dopa therapy for Parkinson's.** Geriatrics. 36(4):34, 39-40, 43, 1981.

Treatment of Parkinson's disease with L-dopa or levodopa is examined and evaluated. The history of the use of L-dopa and discovery of means of maximizing the therapy by combination with dopadecarboxylase inhibitors is discussed. Research which showed no difference between sinemet and madopar as combination drugs for such maximized therapy is cited. Parkinson patients show initial gains on L-dopa therapy, but, although long-term studies show patient maintenance above baseline levels, a general decline is seen in patient's condition over time. Reasons for such regression are discussed. 10 references.

004466 Kral, V. A. University of Western Ontario, London, Ontario N6A 5A5, Canada **Psychopharmacotherapy of sexual disorders in the aged.** Modern Problems of Pharmacopsychiatry. 15:174-181, 1980.

Sexual difficulties presented at a geropsychiatric practice by aged men and women are discussed along with implications for psychopharmacotherapy. Sexual disorders in the male include impotence or fear of impending impotence, increases or decreases in sexual activity as a result of mental disorders (endogenous depression, mania, paranoid psychosis), and pedophilia. Female sexual disorders include psychological difficulties relating to menopause, side-effects of psychiatric disorders such as late paranoid psychoses, local and systemic diseases, and masked neurotic depression. It is suggested that psychopharmacological agents have proved of great help in treating sexual disorders in the elderly, but that most of the problems are of psychogenic origin and require psychotherapy as the treatment of choice. Minor tranquilizers or small dosages of antidepressants may accompany such treatment. Antidepressants, major tranquilizers, and lithium carbonate are indicated in cases of major psychiatric illness, and sexual disorders which form part of a dementing process are also easily controlled by drug medication, although the underlying brain process is usually not influenced by it. 13 references.

004467 Kreek, M. J.; Schecter, A. J.; Gutjahr, C. L.; Hecht, M. no address **Methadone use in patients with chronic renal disease.** Drug and Alcohol Dependence. 5:197-205, 1980.

Methadone disposition was studied in three patients receiving chronic methadone treatment and having chronic renal disease: one oliguric patient during peritoneal dialysis, one anuric patient on hemodialysis, and one patient following renal transplantation. In all three patients plasma levels of methadone remained within the desired therapeutic range (0.09 to 0.68mcg/ml) for the doses received (40 to 50mg/day). Elimination of methadone and its metabolites was almost exclusively by the fecal route in the anuric patient. Less than 1% of the daily dose was removed by peritoneal dialysis or hemodialysis. There was no laboratory or clinical evidence for accumulation of either methadone or its metabolites, suggesting that methadone is an appropriate narcotic to use in patients with renal disease. (Journal abstract)

004468 Krzyminski, Stefan. Szpital Psychiatryczny, woj. Zielonogorskie, 66-212 Ciborz, Poland **/Scopolamine in cholinolytic treatment./** Skopolamina w leczeniu cholinolitycznym. Psychiatria Polska. 14(6):635-640, 1980.

An overview of the literature on the use of scopolamine in cholinolytic treatment discusses the application of the drug in psychotherapy since 1949. It has been found that the drug acts negatively on the mechanism of memory and learning abilities. Contraindications for prescribing the drug are: fever; kidney, liver, and lung diseases; and diseases of the stomach and the duodenum. The drug is recommended in all schizophrenic syndromes, maniacal states of differentiated etiology, and paranoia. The use of scopolamine in cholinolytic treatment recommends itself through the simplicity of method, the facility of application, the rarity of complications, and the possibility of quick intervention through the application of physostigmine or galantamine. 22 references.

004469 Lambert, Nadine M.; Sandoval, Jonathan; Sassone, Dana M. University of California, Berkeley, CA 94720 **Prevalence of hyperactivity and related treatments among elementary school children.** In: Gadow, K., Psychosocial aspects of drug treatment for hyperactivity. Boulder, CO, Westview, 1979. 479 p. (p. 249-291).

Results are presented from a survey of a large representative sample of elementary school children in public and private schools to estimate the prevalence of hyperactivity and the incidence of cerebral stimulant use and other treatment modalities for hyperactivity. The ages at which children's problems were first noted and those at which help was initially sought were determined, as well as the number of professionals involved over time in the treatment process. The findings indicate, in contrast to media reports, that large numbers of children are forced to take amphetamines in order to stay in school, that stimulant medication is used rarely, and that it is only one of several possible interventions which are recommended or tried in individual cases. The data also do not support the view that there are more hyperactive children in the 1970s than there were in an earlier period. It is shown that once they are identified as hyperactive, they do not continue to be defined as hyperactive throughout the elementary school years, and that there is a dynamic interaction of the child with his environmental systems which may be modified successfully during treatment for hyperkinesis. 25 references.

004470 Lepage, D. no address **/Child psychopharmacology./** La psychopharmacologie chez l'enfant. Feuillets Psychiatriques de Liege. 12(1-2):27-47, 1979.

The indications for and limits of chemotherapy in child psychiatry are discussed. Chemotherapy has tended to hold a secondary place in child psychiatry because of resistance by doctors and because of the unknown long-term effects of various medicines. The use of chemotherapy implies a certain form of doctor-patient relationship which is best approached phenomenologically. Chemotherapy has been used in children with behavioral problems such as hyperkinesis and functional disorders such as stuttering, enuresis, and tics. It has also been used in cases of mental retardation and psychosis. A complete evaluation of the effectiveness of chemotherapy for children has not yet been made, although it has been found to be definitely effective in treating hyperkinesis and enuresis. 82 references.

004471 Markianos, M.; Hadjikonstantinou, M.; Sfagos, C. Athens University Medical School, Dept. of Psychiatry, Eginition Hospital, Vass. Sophias 74, Greece **Normal plasma dopamine-beta-hydroxylase in non-treated and treated Parkinson patients.** Acta Neurologica Scandinavica. 63(4):267-272, 1981.

Plasma dopamine-beta-hydroxylase activity (DBH) was estimated in 50 drug free Parkinson patients, 30 of whom had never been treated, in 26 patients treated chronically with L-Dopa, and in 44 controls. In disagreement with other reports, no differences were found among the groups and no change in the enzyme activity occurred after treatment, although urinary homovanillic acid increased 20 fold. Low DBH activities could not be attributed to the age of onset or duration of illness, main symptom, depression, autonomic disturbances, or duration of drug treatment. Findings indicate that patients with dementia associated with their illness showed low enzyme activities. 14 references. (Author abstract modified)

004472 Menia, Azzedine; Viaud, Pierre; Baron, Jean-Bernard. Dept. de posturographie, C.H.U., Sainte-Anne, l, rue Cabanis, F-75674 Paris Cedex 14, France **/Dose effect of D.E.A.E. on subjective problems, vertigo, ●depression,● asthenia, cephalalgia, and tonic postural activity problems recorded with statokinesimeter in postconcussional syndrome./** Effet-dose du D.E.A.E. sur les troubles subjectifs vertiges, ●depression●, asthenie, cephalees, et les troubles de l'activite tonique posturale enregistres au statokinesimetre, du syndrome post-commotionnel des traumatises craniens ou cranio-cerv. Psychologie Medicale. 12(10):2255-2263, 1980.

The effects of D.E.A.E. (cerebrol, an acetylcholine precursor) on disturbances resulting from head or whiplash injuries were studied. Twenty patients with such injuries were administered 1.5g or 3g daily of D.E.A.E. for a period of 20 days, and the following disturbances were measured: tonic postural activity problems, vertigo, asthenia, depression, and cephalalgia. Results indicate that the subjects who received 1.5g of D.E.A.E. demonstrated: 43% variation in the statokinesigram, 60% normalization of convergence, 50% normalization of index deviation, 44% improvement of cephalalgia, 50% improvement of vertigo, 48% improvement of asthenia, and 61% improvement of depression. The subjects who received 3g of D.E.A.E. did not show such good results. Minimal lesions of the cholinergic structure in the midbrain were believed to exist in the subjects. The danger of overdose in D.E.A.E. therapy is emphasized. 4 references. (Journal abstract modified)

004473 Morgan, David D.; Robinson, J. D.; Mendenhall, C. L. V.A. Medical Center, 3200 Vine St., Cincinnati, OH 45220 **Clinical pharmacokinetics of chlordiazepoxide in patients with alcoholic hepatitis.** European Journal of Clinical Pharmacology. 19(4):279-285, 1981.

The clearance of chlordiazepoxide (CDX) from the systemic circulation was studied in 20 human Ss, including 15 patients with alcoholic hepatitis and five normal volunteers. The half-life for the appearance of the drug in the systemic circulation was found to increase exponentially with age, and half-life was independent of the presence of alcoholic hepatitis. The metabolic clearance of CDX was significantly lower in the patients than in the normal Ss. Multiple regression analysis of the clearance data of the initial and followup studies show a significant correlation between clearance and the variables age, albumin, and lactate dehydrogenase. This relationship suggests that over a short period of time (where age can be considered constant) changes in albumin and lactate dehydrogenase could be potentially useful in predicting clearance changes in a single individual. 34 references. (Author abstract modified)

004474 no author. Office of Scientific and Health Reports, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20205 **Fact sheet: Tourette syndrome.** Bethesda, MD, NIH Pub. No. 80-2163, 1980. 1 p.

Brief information about the Gilles de la Tourette syndrome, a neurological disorder characterized by involuntary muscular movements, uncontrollable vocal sounds, and inappropriate words, is presented. These multiple tics usually begin when the patient is between 2 and 16 years old, and males are afflicted about three times more often than females. The disorder is thought to be caused by a chemical abnormality in the neurotransmitter system by which the brain regulates movement and behavior. Physicians have had some success treating Tourette syndrome patients with haloperidol, also known as Haldol, which suppresses symptoms for many patients, but does not cure the condition. Psychotherapy may help the patient cope with the disorder, and deal with the social and emotional problems that sometimes accompany it. Research being conducted on the disorder, the prognosis for patients, the best educational setting for patients, and the contribution of a voluntary advocacy organization are addressed.

004475 no author. no address **Asthma therapy may undercut kids at school.** Medical World News. 22(3):37, 41, 1981.

Research conducted at the National Jewish Hospital-National Asthma Center on the causes of learning problems in asthmatic children is reported. In a study of 94 asthmatic children ages 9 to 18-years-old, it was found that they did better on standard tests of memory and learning ability as the effects of corticosteroid medication wore off. The findings are regarded as preliminary and future research must compare these results with tests of nonasthmatic children taking steroids for other reasons.

004476 no author. no address **Levodopa: long-term impact on Parkinson's disease.** British Medical Journal. No. 6262:417-418, 1981.

Research concerning the long-term impact of levodopa treatment on Parkinson's disease is reviewed. It is noted that the initial response to levodopa in parkinsonism is markedly favorable in three quarters of patients. However, after 2 years of treatment, the proportion of patients who maintain the initial level of improvement decreases, and complications of the drug steadily increase. Two common problems are dyskinetic movements and on/off swings in performance. Psychiatric complications are the most serious side-effects of levodopa, often necessitating reduction or withdrawal of treatment. Suggestions for reducing side-effects are described. 8 references.

004477 Norman, Trevor R.; Burrows, Graham D.; Bianchi, Geoffery N.; Maguire, Kay P.; Wurm, Jeremy M. E. Dept. of Psychiatry, University of Melbourne, Parkville, Victoria 3052, Australia **Doxepin plasma levels and anxiolytic response.** International Pharmacopsychiatry. 15(4):247-252, 1980.

A study of 23 patients (16 females, 7 males), diagnosed as suffering from anxiety, was carried out using a flexible dosage regimen of doxepin. Hamilton Anxiety Rating Scale scores were assessed on days 0, 7, 14, and 21, and plasma doxepin and desmethyldoxepin concentrations were analyzed from blood samples taken on days 7, 14, and 21 of the trial. No simple correlation between the Hamilton score at day 21 and plasma doxepin concentration (rs=-.099, p greater than .05; n=19) or plasma desmethyldoxepin concentration (rs=.339, p greater than .05; n=19) was obtained. The sum of doxepin and desmethyldoxepin concentrations was not correlated with the Hamilton score at day 21 (rs=.276, p greater than .05; n=19). No correlation of doxepin, desmethyldoxepin, or total concentrations and Hamilton score was found on days 7 or 14 of the trial. 15 references. (Author abstract)

004478 Oosterveld, W. J. Vestibular Dept. of the O-R-L Clinic, Academic Hospital Wilhelmina Gasthuis, Eerste Helmerstraat 104, NL-1054 EG Amsterdam, The Netherlands **The efficacy of piracetam in vertigo: a double-blind study in patients with vertigo of central origin.** Arzneimittel-Forschung. 30(11):1947-1949, 1980.

The clinical efficacy of piracetam was assessed in 22 patients with vertigo of central origin (posttraumatic, psychogenic, ecileptogenic, and hypertensive vertigo were excluded). In a double-blind, switchback design, piracetam reduced symptoms significantly more than did placebo. Ss reported that piracetam affected vertigo, motility disturbances, and vitality, but it did not affect sleep. The effect of piracetam is explained by enhanced control of the cerebral cortex on subordinated vestibular centers. 16 references. (Author abstract modified)

004479 Pechadre, J. C.; Beudin, P.; Devoize, J. L.; Gibert, J. Lab. d'Electroencephalographie Clinique, Hotel-Dieu, Cntr. Hospitalier Regional, B.P. 69, F-63003 Clermont-Ferrand Cedex, France **/Antiepileptic effect of clobazam in Lennox-Gastaut syndrome./** Utilisation du clobazam comme anti-epileptique dans le syndrome de Lennox et Gastaut. Encephale. 7(2):181-190, 1981.

The antiepileptic effect of a special benzodiazepine (1,5-benzodiazepine or clobazam) on a homogeneous sample of 26 patients suffering from the epileptic encephalopathies syndrome was studied. Fifteen days after the beginning of the treatment 15 of the 26 patients (57%) were benefitting from the therapy. More than 1 year later, 10 patients (42%) were still being treated succesfully. The classical exhaustion side-effect from benzodiazepines seems marked at 1 and 6 months. Although watchfulness problems have been found approximately as often as with other benzodiazepines, it was apparent that these side-effects were less severe. The use of clobazam or nitrazepam brought about an improvement in the state of watchfulness. Four patients already receiving polychemotherapy experienced the classical intolerance phenomena. To avoid this problem, clinical surveillance during the first few days is recommended. Care should be taken when clobazam is used in conjunction with strong doses of dipropylacetic acid. 10 references. (Journal abstract modified)

004480 Philipp, M. Neuro-Psychiatrische Abteilung, Universitatsklinik Mainz, Mainz, West Germany **/Psychotic excitement in medical emergencies./** Psychotische Erregtheit im arztlichen Notfalldienst. Medizinische Welt. 30:1436-1438, 1979.

Several legal viewpoints and important pharmacological and psychotherapeutical measures taken in the treatment of psychotic excitement in medical emergencies are discussed. It is suggested that three substances, Neurocil, Haldol, and Valium, are sufficient to control all psychotic conditions of excitement in manias exhibited in katogenic and frenzied hallucinatory schizophrenias, and in exogenic psychoses. (Journal abstract modified)

004481 Rabending, G.; Fischer, W,; Arndt, R.; Bohl, I.; Bruckner, H.-J.; Cammann, G.; Du Chesne, H.-J.; Hobusch, D.; Knaape, H.-H. Nervenklinik des Bereiches Medizin, Ernst-Moritz-Arndt-Universitat, Ellernholzstrasse 1/2, DDR-22 Greifswald, German Democratic Republic **/Treatment of epilepsies with clonazepam (Antelepsin)./** Die Behandlung der Epilepsien mit Clonazepam (Antelepsin). Psychiatrie, Neurologie und Medizinische Psychologie. 31(8):472-482, 1979.

Clonazepam was tested in a total of 179 epileptic patients from eight institutions for a period of 180 days. One hundred sixty nine of the patients previously had been treated unsuccessfully with standard medication. Typical abcences and attacks of West syndrome and Lennox syndrome responded very well to treatment. Favorable effects also were produced in cases of partial or focal epilepsy. The most noticeable side-effect was fatigue, though balance disorders, sensations of dizziness, and muscular weakness also were reported. The frequency of side-effects decreased during the course of therapy. An EEG examination revealed a significant increase in beta-waves and a significant decrease in 3 Hz spike and wave complexes. (Journal abstract modified)

004482 Reisberg, Barry; Ferris, Steven H.; Gershon, Samuel. Geriatric Study and Treatment Program, Dept. of Psychiatry, N.Y.U Medical Center, 550 First Ave., New York, NY 10016 **An overview of pharmacologic treatment of cognitive decline in the aged.** American Journal of Psychiatry. 138(5):593-600, 1981.

The pharmacological treatment of cognitive decline/senile dementia in the aged is discussed, with emphasis on the most widely known substances for alleviating the mental and behavioral symptoms. These substances include: cerebral vasodilators, Gerovital H3, psychostimulants, nootropics, neuropeptides, and neurotransmitters. It is contended that the rationale for the choice of specific agents has shifted as conceptions on the origins of cognitive decline have changed, and that current knowledge indicates that most deterioration occurs independently of arteriosclerotic vascular changes. Substances currently being investigated for their effects on brain electrophysiology, in neurohumoral processes, or on central neurotransmitters, are seen as having promise. 96 references. (Author abstract modified)

004483 Renshaw, D. C. Dept. of Psychiatry, Sexual Dysfunction Clinic, Loyola University of Chicago, 2160 South First Ave., Maywood, IL 60153 **Pharmacotherapy and female sexuality.** Modern Problems of Pharmacopsychiatry. 15:145-157, 1980.

Common forms of female sexual dysfunction are discussed, along with implications for pharmacotherapy and sex therapy. These dysfunctions include: 1) no sexual desire (parasympathetic and higher brain center involvement); 2) primary or secondary anorgasmia (involvement of sympathetic and higher brain centers); 3) dyspareunia (involvement of local or higher centers); and 4) vaginismus (involvement of local or higher centers). The aphrodisiacs and medications that may be useful in enhancing sexual enjoyment or overcoming the dysfunctions include: alcohol, hormones, stimulants, antidepressants, tranquilizers, hypnotics and sedatives, lithium, L-dopa and PCPA, street drugs (marihuana, psychedelics, and narcotics), bromocryptine, and miscellaneous compounds (perfumes and placebos). Suggestions are made for carefully controlled research to investigate a variety of myths that have arisen from the drug culture and it is emphasized that psychological as well as physiological factors should be considered in addition to pharmacotherapy. 21 references.

004484 Schimmel, K. C. Kurklinik Kronprinz, Prien, West Germany **/The treatment of insomnia through homeopathy in a clinic./** Die Behandlung von Schlafstorungen mit Mitteln der Naturheilverfahren in einer Klinik. Physikalische Medizin und Rehabilitation. 20:549-552, 1979.

The treatment of insomnia through homeopathy in a clinic, and various causes of insomnia were examined. Originating from either organic or psychological influences, patients in a clinic were treated both physically and homeopathically. A number of homeopathic drugs are recommended. (Journal abstract modified)

004485 Shapiro, Arthur K.; Shapiro, Elaine. Tic and Tourette Laboratory and Clinic, Mount Sinai Medical School, 1 Gustave Levy Place, New York, NY 10029 **Do stimulants provoke, cause, or exacerbate tics and Tourette syndrome?** Comprehensive Psychiatry. 22(3):265-273, 1981.

The effects of stimulants on tics and Tourette syndrome (TS) were examined in a review of the literature and in a clinical study of patients with tics or TS. The literature provides virtually no evidence that stimulants cause or provoke TS, and inadequate evidence that stimulants in clinically appropriate doses can cause tics in previously asymptomatic patients or exacerbate tics in patients with preexisting tics or TS. Methylphenidate and haloperidol in combination did not increase tics in 42 patients treated for concomitant hyperactivity and TS, nor in most of the 62 TS patients treated with stimulants for various adverse effects of haloperidol. Although tics may increase in some patients at a dose of methylphenidate that simultaneously decreases lethargy, amotivation, and impaired cognition, there is no net gain in the therapeutic to toxic ratio, the effect is short lived, and potential benefits outweigh disadvantages. Observations fail to support the catecholamine hypothesis for tics and TS. 18 references. (Author abstract modified)

004486 Sobczyk, Piotr; Jena, Krystyna; Klir, Teresa. I Klinika Psychiatrii S1. AM, Grunwaldzka 48, 42-700 Lubliniec, Poland **/A comparative evaluation of the efficacy of some therapeutic methods used in delirium tremens./** Porownawcza ocena skutecznosci niektorych metod leczenia majaczenia drzennego. Psychiatria Polska. 14(5):481-486, 1980.

Therapeutic methods used from 1970 to 1971 and from 1977 to 1978 to treat patients with delirium tremens were compared. It was found that only neuroleptics and tranquilizers (chlordiazepoxide, diazepam, and chlormethiazol) were used alone or in combinations. The 3.8% mortality rate was not related to delirium tremens in 50% of the cases, but to severe somatic illnesses. No cases of death were noted in the group of patients receiving chlormethiazol orally, whereas the length of duration of delirium tremens did not appear to depend significantly on the kind of therapeutic method applied. 19 references. (Journal abstract modified)

004487 Sorel, L.; Mechler, L.; Harmant, J. Centre William Lennox, Ottignies, Louvain-la-Neuve, Belgium **/A comparative study of intravenous lorazepam and clonazepam in status epilepticus./** Etude comparative de l'injection intraveineuse de lorazepam et de clonazepam dans les etats de mal epileptique. Acta Neurologica Belgica. 80(6):368-379, 1980.

The use of lorazepam and clonazepam in treating epilepsy was compared. Sixty one Ss received a total of 129 injections of lorazepam (4 to 10mg) and/or clonazepam (1mg). Results show that lorazepam had very favorable results in three quarters of cases and significantly improved the EEG in both primary and secondary generalized epilepsy and in partial epilepsy, although results were somewhat better in secondary generalized epilepsy. Results with clonazepam were approximately the same, but lorazepam showed slightly better results for the EEG, and clonazepam showed slightly better results for clinical factors. The disadvantage of this treatment is decreased awareness with lorazepam (66% of cases) and with clonazepam (74% of cases). 12 references.

004488 Strandjord, R. E.; Aanderud, S.; Myking, O. L.; Johannessen, S. I. Dept. of Neurology, 5016 Haukeland Sykehus, Bergen, Norway **Influence of carbamazepine on serum thyroxine and triiodothyronine in patients with epilepsy.** Acta Neurologica Scandinavica. 63(2):111-121, 1981.

The influence of carbamazepine (CBZ) on serum thyroxine (T4) and triiodothyronine (T3) concentrations of patients with epilepsy was investigated. In 42 patients on long-term CBZ treatment, T4, free T4 index (FT4I), and T3 concentrations in serum were significantly lower than in control Ss, while T3 uptake (T3U) and thyrotropin (TSH) concentrations did not differ between patients and control Ss. In 12 patients starting on CBZ, mean T4, calculated FT4I, and thyroxine binding globulin (TBG) were reduced 1 to 5 months later compared to the initial levels. Thus, CBZ reduced thyroid hormones, TGB, and FT4I. A CBZ-induced increase in conversion and metabolism of the thyroid hormones could explain this effect. The normal T3U values and decreased concentrations of TBG make a competitive CBZ binding to TBG less probable. Although the thyroid hormone levels were found lowered in the patients, all remained clinically euthyroid during the period of the study. 19 references. (Author abstract modified)

004489 Su, C. Y.; Lin, C. S.; Peng, C.; Cheng, C. S.; Loh, H. H.; Li, C. H.; Way, E. L. Taipei Medical College, Taipei, Taiwan **Suppression of morphine abstinence in heroin addicts by beta-endorphin.** Advances in Biochemical Psychopharmacology. 22:503-509, 1980.

The effects of beta-endorphin on morphine abstinence in heroin addicts were assessed under conditions where physical dependence could be established and quantified. The effectiveness of beta-endorphin in attenuating morphine abstinence effects was clearly established on a double-blind basis in four Ss. Although a placebo response was noted, its effects were mild and transient. The potency of beta-endorphin per mg appears comparable to that of morphine, suggesting that on a molar basis, beta-endorphin is at least 10fold more potent than morphine. 11 references.

004490 Sundaram, Yamuna; Valmikinathan, K. Dept. of Neurochemistry, Institute of Neurology, Madras Medical College, Madras 600 003, India **Biochemical studies of human epileptics during anticonvulsant therapy.** Neurology India. 28(4):225-233, 1980.

Metabolic events in Indian epileptics on single doses or combinations of anticonvulsant drugs were investigated. Biochemical screening of 70 epileptics and a group of Ss suffering from neurological disorders indicate a greater incidence of single toxic side-effects than of multiple effects. The incidence of low phosphorus levels was noted following long-term therapy, wheras elevated alkaline phosphatase was observed in short-term therapy. It was also found that phenobarbital, alone, has a pronounced effect on alkaline phosphatase, as compared to dilantin. 13 references. (Author abstract modified)

004491 Suzuki, Jinichi. no address **A clinical evaluation of the effects of a new psychotropic agent, mexazolam (CS-386) on psychosomatic diseases and neurosis: a comparative study with oxazolam, using the double-blind method.** Japanese Journal of Psychosomatic Medicine. 20(4):301-316, 1980.

The effects of a new benzodiazepino oxazole agent, mexazolam, on the mental symptoms of anxiety, tension, and insomnia, and the physical symptoms of dizziness, nausea, chest pain, and dullness of the head were examined. Subjects were 165 patients with either psychosomatic diseases or various kinds of neuroses. The experiment was double-blind using oxazolam as a control. The rate of final global improvement was 75.6% in the cases using mexazolam and 63.8% in cases using oxazolam. Mexazolam showed marked effectiveness against essential hypertension and peptic ulcer and irritable colon and autonomic nervous dystonia. Anxiety neurosis and organ neurosis are considered suitable indications for mexazolam. Side-effects of drowsiness and giddiness were seen more frequently with mexazolam than in the control group. Findings indicate mexazolam is a more effective drug than oxazolam and its usefulness for psychosomatic disease and neurosis is confirmed. (Journal abstract modified)

004492 Wilkie, Frances L. Dept. of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, Seattle, WA 98195 **Blood pressure and cognitive functioning.** In: Haynes, S., Second conference on the epidemiology of aging. Washington, GPO, NIH Pub. No. 80-969, 1980. 387 p. (p. 105-126).

The effects upon cognitive functioning of antihypertensive drugs and other techniques used to lower blood pressure, differential rates of decline in performance as a function of blood pressure level, and possible underlying mechanisms accounting for the relationship between performance and blood pressure are considered, based on a review of the literature. The three general classes of antihypertensive agents include: diuretics, adrenergic nervous system inhibitors, and vasodilators. Some findings suggest that antihypertensive drugs (vasodilators) may enable hypertensives to maintain their level of cognitive functioning at least well as do their normotensive age peers. Research is cited concerning: the acute effects of lowering blood pressure upon psychomotor response speed using a serial reaction time task, the effect of propranolol on the performance of normotensive young individuals, side-effects of antihypertensive drugs, biofeedback training, and performance on intelligence tests of borderline high and high blood pressure Ss. The underlying mechanisms of cerebral blood flow and psychosocial stress which may affect performance of hypertensives are addressed. A discussion follows the text of the article. 72 references.

004493 Yesavage, Jerome A.; Tinklenberg, Jared R. Veterans Administration Medical Center, Palo Alto, CA 94304 **Single-case study of clinical response to high-dose ergot alkaloid treatment for dementia. Preliminary report.** Gerontology. 27(1,2):76-78, 1981.

A case history of senile dementia of the Alzheimer's type that was treated with dihydroergotoxine mesylate (DEM) is reported. The patient was a 68-year-old male who showed higher order intellectual deficits. There was no evidence of depression on psychological testing or rating scales and the patient failed to respond to trials of antidepressants and phenothiazines. The patient was evaluated frequently on the same outcome measures while drug dosage varied from 0 to 6 mg. Results show a significant drug effect. The optimal dosage of DEM and its mechanism of action are uncertain. It is possible that this patient suffers from a rare type of biochemically based dementia which is specific in its response to DEM. More information is needed on the pathophysiology of dementias and the efficacy of some of the treatments. 7 references.

004494 Zalejski, Stanislaw; Pakszys, Waldemar. Klinika Neurologii CKP WAM, Szaserow 128, 00-909 Warszawa, Poland / **The effect of diphenylhydantoin on EEG curves in epileptics.**/ Wplyw dwufenylhydantoiny (DPH) na zapis EEG u chorych na padaczke. Neurologia i Neurochirurgia Polska. 14(6):617-620, 1980.

Clinical and EEG investigations were performed, and the serum diphenylhydantoin (DPH) level was determined in a homogenous group of 32 hospitalized males aged 20 to 22. Spectrophotometric determination of the drug was found to be useful. The effect of the therapeutic DPH level on regression of abnormal EEG tracings was demonstrated to be statistically significant. Absence of improvement or exacerbation of EEG changes should arouse the suspicion that levels of 10 to 20mcg/ml of serum DPH have not been attained or have been exceeded. 17 references. (Journal abstract modified)

004495 Zysset, T.; Rudeberg, A.; Vassella, F.; Kupfer, A.; Bircher, Johannes. Bircher: Dept. of Clinical Pharmacology, University of Berne, Murtenstrasse 35, CH-3010 Berne, Switzerland **Phenytoin therapy for epileptic children: evaluation of salivary and plasma concentrations and of methods of assessing compliance.** Developmental Medicine and Child Neurology. 23(1):66-75, 1981.

Phenytoin concentrations in mixed saliva and parotid saliva from 22 children, from ages 6 to 15 who were receiving phenytoin therapy for epilepsy were compared with plasma levels from blood obtained at the same time. For mixed saliva, the saliva to plasma concentration ratio was .11 plus or minus .04 and in parotid saliva it was .10 plus or minus .06. Compliance was studied in 13 children, each receiving between three and seven different quantities of phenytoin. Clinical judgment about compliance agreed with the two laboratory measures. An analysis of the relationship between plasma concentration and dosage is proposed as a practical method of assessing compliance. 14 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

004496 Brooks, Alexander D. Rutgers Law School, 15 Washington Street, Newark, NJ 07102 **The constitutional right to refuse antipsychotic medications.** Bulletin of the American Academy of Psychiatry and Law. 8(2):179-221, 1980.

An overview of the constitutional right to refuse treatment with antipsychotic medication is presented. The legal grounds for the right to refuse are summarized, and issues relating to standards and procedures in medication refusal cases are discussed. Issues which must be addressed in considering whether courts should intervene and establish a limited constitutional right to refuse include: the benefits of medication; the costs of medications in terms of their side-effects, the nature and seriousness of side-effects; patient reactions to side-effects, including psychiatric reactions; the potential for abusive prescription practices; respect for patient autonomy; and patient competence to make treatment decisions. In the Rennie decision, the court recognized the right to refuse medication, but made it subject to two qualifications: the patient is not permitted to refuse if he is incompetent or if he is dangerous to himself or others. Difficulties in the interpretation of these two qualifications are considered, and procedural guidelines for determinations of competency and dangerousness/emergency are outlined. The use of the independent psychiatrist to review medication decisions, the role of the patient advocate, and the least restrictive alternative doctrine are discussed. The psychiatric reaction to the right to refuse medication and arguments against such a right also are considered. 116 references.

004497 Hofmann, Albert. no address **LSD: my problem child.** New York, McGraw-Hill, 1980. 210 p. $9.95.

The story of the discovery of lysergic acid diethylamide, LSD-25, and of events following its discovery are related by its originator. The psychotherapeutic uses of LSD are delineated, but its discoverer appears to be more interested in its use in terminal illness and as a stimulant to creativity. Accounts are provided of meetings with Timothy Leary, and of contact with Aldous Huxley who was injected with LSD in his dying hours. It is argued that what is needed today is a fundamental reexperience of the unity of all living things. The potential of LSD is posited, and the drug is envisioned as a sacred drug which, if used under suitable conditions, in medical practice and in conjunction with medication, might in the future make a wonder child of the problem child.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

004498 Adler, David S. University Hospital (H-765), University of California Medical Center, San Diego, CA 92103 **Use of plasma concentration determinations.** Clinical Toxicology. 14(2):147-150, 1979.

The use of phenytoin plasma levels in establishing the therapeutic regimen, adjusting therapy in the presence of drugs that may influence phenytoin disposition, assessing compliance, and validating suspected toxicity is discussed. Special requirements of patients with end stage renal disease or low albumin diseases are considered. The importance of the time of sampling is explained, and it is suggested that samples should generally be drawn at the end of the dosing interval, just prior to the next dose. 8 references.

004499 Arato, Mihaly. National Institute for Nervous and Mental Diseases, Budapest Pf 1, H-1281, Hungary **Promethazine and diazepam potentiate the haloperidol induced prolactin responses.** Communications in Psychopharmacology. 4(4):317-322, 1980.

The effect of promethazone, diazepam, and diethazine on haloperidol-induced prolactin response was investigated in a single dose study. These drugs are generally used for treatment of drug-induced extrapyramidal symptoms; i.e., they can anatgonize the effect of neuroleptics on nigrostriatal dopaminergic systems. Promethazine and diazepam significantly enhanced the haloperidol induced prolactin secretion. According to these results, these drugs potentiate the effect of haloperidol on hypothalamic/pituitary dopaminergic systems. This finding supports the view that differential regulatory mechanisms exist for various dopaminergic regions and/or for the regional specificity of the actions of promethazine and diazepam. Diethazine had no effect on haloperidol induced prolactin secretion. 14 references. (Author abstract modified)

004500 Becker, D.; Creutzfeldt, O. D.; Schwibbe, M.; Wuttke, W. Wuttke: Dept. of Neurobiology, Max-Planck-Institute for Biophysical Chemistry, Am Fassberg, D-34 Gottingen Nikolausberg, West Germany **Electrophysiological and psychological changes induced by steroid hormones in men and women.** Acta Psychiatrica Belgica. 80(5):674-697, 1980.

The effects of hormonal changes during the menstrual cycle and of oral contraceptives on the EEG, heartrate, and a number of performance tasks were investigated in 16 female subjects. Powerspectral analysis in the EEG revealed significantly increased alpha frequencies and heartrates during the luteal phase of the menstrual cycle whereas the mean theta frequency and power decreased. A number of psychological test variables, such as reaction time to a tone, to a flickering light, and to a color/tone sequence and the time to solve simple arithmetic problems were shorter at the periovulatory time. Another minimum was reached during the perimenstrual phase. The flicker/fusion frequency was higher during these two periods. No such effects were observed when the same Ss were treated with oral contraceptives. It is concluded that the phenomena observed during the luteal phase of the cycle may be the expression of a slight general arousal effect, possibly mediated by progesterone via the noradrenergic system. Results of a subsequent double-blind study are also reported in which 30 males were treated with a gestagenic compound, an estrogenic compound, an androgenic substance, or with placebo. Results show that only treatment with the progestational compound produced significant changes in the EEG and the performance tests. 15 references. (Author abstract modified)

004501 Boulenger, J.-Ph.; Zarifian, E. Zarifian: Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France **/Neuroleptic-tricyclic antidepressant combination: pharmacological aspects and therapeutic interest./** L'association neuroleptique-antidepresseur tricyclique: aspects pharmacologiques et interet therapeutique. Encephale. 7(1):5-28, 1981.

The use of neuroleptics in combination with tricyclic antidepressants is reviewed. Although different psychotropic drugs are frequently prescribed simultaneously, only a few studies have been done to verify the usefulness of this technique. Neuroleptics and tricyclic antidepressants appear to have opposite pharmacological and biochemical properties. However, controlled clinical trials have not demonstrated therapeutic antagonism between these two types of drugs. On the other hand, although pharmacokinetic data show that neuroleptics decrease the metabolism of tricyclic antidepressants, the therapeutic advantage of combining them has not been proved. Methodological issues raised by these studies are also discussed. 114 references. (Journal abstract modified)

004502 Bowers, Malcolm B., Jr.; Heninger, George R. Dept. of Psychiatry, Yale University School of Medicine, 25 Park St., New Haven, CT 06519 **Cerebrospinal fluid homovanillic acid patterns during neuroleptic treatment. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-28216, 1980. 14 p.

A group of 24 psychotic patients were studied at two points during continuous neuroleptic treatment. Thirteen patients showed a tolerance pattern with respect to cerebrospinal homovanillic acid following probenecid, while 11 showed a nontolerance pattern. Patients who developed tolerance had significantly fewer symptoms and Parkinsonian side-effects at about the fifth week of treatment. The findings have implications for other studies which indicate that tolerance patterns reflect a decrease in dopamine metabolites during chronic neuroleptic treatment, and that there may be regional brain differences in the development of this pattern during chronic treatment. 24 references. (Author abstract modified)

004503 Buvat, J.; Racadot, A.; Buvat-Herbaut, M.; Lemaire, A.; Gossati, P. Service d'Endocrinologie et de Diabetologie, Centre Hospitalier Universitaire de Lille, Ave. du Professeur Laguesse, F-59037 Lille, France **/Basal prolactinaemia and responses to TRH and sulpiride in different categories of male sexual dysfunctions./** Prolactinemie basale et reponses au TRH et au sulpiride dans diverses categories de dysfonctions sexuelles masculines. Acta Psychiatrica Belgica. 80(4):487-493, 1980.

Serum testosterone levels and serum prolactin levels in 435 sexually dysfunctioning males were studied. Prolactin response to 200mcg of thyrotropin releasing hormone (TRH) was studied in 41 cases, and prolactin response to sulpiride was studied in 38 cases. Results show that serum prolactin levels were excessively high in three cases of impotence and one case of anejaculation; prolactin was mildly increased in 3.7% of the cases of impotence and 17% of the cases of premature ejaculation. Mean prolactin level was lower in anejaculatory and impotent males than in normal males. Testosterone was lower in anejaculatory males than in normal males, impotent males, and premature ejaculators. The area under the curve for prolactin response to TRH was lower in anejaculatory and impotent males than in normal males and premature ejaculators. Prolactin response to sulpiride showed no difference from that of normal males. 10 references. (Journal abstract modified)

004504 Chasseaud, L. F.; Taylor, T.; Brodie, R. R. Dept. of Metabolism and Pharmacokinetics, Huntingdon Research Center, Huntingdon, England **Prazepam metabolism in female**

subjects. Journal of Pharmacy and Pharmacology. 32(9):652-653, 1980.

The metabolism of prazepam was studied in fasting female volunteers. The peak mean plasma concentration of the metabolite N-desalkylprazepam occurred 12 hours after drug administration, but plasma concentrations remained high for 5 to 24 hours and declined with a mean half-life of 107 hours. Neither prazepam nor N-desalkylprazepam were detected in 24 hour urine or any of the Ss above a detection limit of 2ng/ml; 3-hydroxyprazepam and oxazepam were present, almost totally conjugated. Results suggest that the major metabolic route of prazepam, like that of diazepam, is N-dealkylation followed by hydroxylation. 11 references.

004505 Dry, J.; Ardaillou, R.; Pradalier, A.; Isaac, R.; Piquet, V. Hopital Rothschild, Service de Medecine interne, Boulevard de Picpus 33, F-75012 Paris, France **/Hormonal stimulation after injection of thyrotrophin releasing factor (TRF) and 1-24 ACTH in patients following chronic treatment with neuroleptics: preliminary study./** Resultats des tests de stimulation par le facteur de liberation de la thyrostimuline (TRF) et par le fragment 1-24 de l'hormone corticotrope chez des sujets traites au long cours par des neuroleptiques: etude preliminaire. Acta Psychiatrica Belgica. 80(5):607-618, 1980.

Fifteen patients on neuroleptic treatment (haloperidol or phenothiazines) and 11 control patients were given thyrotropin releasing hormone (TRH) 250mcg and 1-24 ACTH. Thyroid stimulating hormone (TSH), T3, thyroxin, FT4, prolactin (PRL), and cortisol were measured. Before TRH injection, at baseline, TSH was higher and T3 was lower in the neuroleptics treated group than in the control group. These results suggest the occurrence of a biological hypothyroidism in the group with neuroleptics. PRL was also significantly increased. After TRH injection the response was not significantly different between the groups. Results show cortisol level was lower at baseline and after 1-24 ACTH injections in the groups with neuroleptics. 22 references. (Author abstract modified)

004506 Esler, Murray; Jackman, Graham; Leonard, Paul; Skews, Helen; Bobik, Alex; Korner, Paul. Baker Medical Research Institute, Commercial Road, Prahran 3181, Victoria, Australia **Effect of norepinephrine uptake blockers on norepinephrine kinetics.** Clinical Pharmacology and Therapeutics. 29(1):12-20, 1981.

Norepinephrine (NE) kinetics were studied in normal male Ss after a single 125mg oral dose of desipramine, a neuronal NE uptake blocker. Desipramine reduced plasma NE clearance by about 20% and reduced the rate of spillover of NE to plasma. Disappearance of tritiated NE from plasma after infusion to steady-state was biexponential, with half-times of 2.0 minutes for the rapid removal phase and 34 minutes for the second exponential. The half-time of the rapid removal phase was prolonged by desipramine. In patients with sympathetic nerves damaged by disease (idiopathic peripheral autonomic insufficiency), plasma NE clearance was slowed and the half-time of the rapid removal phase was lengthened. The selective extraneuronal NE uptake blocker, cortisol (500mg i.v.), had no effect in normal Ss on plasma NE clearance or rapid removal half-time. 31 references. (Author abstract modified)

004507 Fornaro, P.; Castrogiovanni, P.; Perossini, M. Clin. Psichiat., University of Pisa, Pisa, Italy **Electroretinography (ERG) as a tool of investigation in human psychopharmacology. Electroretinographic changes induced by a combination of carbi-dopa and levo-dopa.** Acta Neurologica. 2:293-299, 1980.

The electroretinographic (ERG) effects of a combination of levo-DOPA (250mg) and carbi-DOPA (25mg) given per os to 10 healthy male volunteers were studied. A significant decrease in the implicit time of the b-wave was observed 1 and 2 hours after drug administration, whereas an increase in the b-wave amplitude occurred at the same observation times. This increase appeared significant if compared with changes which occurred in a control group treated with diazepam 1 and 2 hours after drug administration. It is concluded that these results may be attributed to a facilitating effect on dopaminergic transmission in the retina. This hypothesis was strengthened by the finding in a previous study that haloperidol, which inhibits such transmission, decreases the b-wave amplitude. (Journal abstract)

004508 Forsman, Lennart. Dept. of Psychology, University of Stockholm, Box 6706, S-113 85 Stockholm, Sweden **Consistency in catecholamine excretion in laboratory and natural settings: correlational and variance components analyses.** Reports from the Department of Psychology, No. 556. Stockholm, University of Stockholm, 1979. 16 p.

Data from 44 healthy male Ss participating in two studies were used to evaluate the consistency of catecholamine excretion as well as changes in the excretion rate across different laboratory and natural situations spaced at intervals of a maximum of 3 months. Correlational analyses showed high consistency of adrenaline excretion under laboratory conditions standardized with regard to degree and kind of activity, regardless of the interval at which measures were taken. For noradrenaline, excretion consistency tended to decrease with increasing time interval. In nonstandardized natural situations the consistency of both amines was rather low. The analysis of various components showed that when situations were similar in terms of degree and kind of activity, the variance due to individuals was large in relation to that due to situations or subject/situation interaction. The variance due to situations was relatively low regardless of the subjects' activity level, whereas variance due to subject/situation interaction increased as the total variance component increased. 21 references. (Author abstract)

004509 Gawel, M. J.; Glover, Vivette; Burkitt, M.; Sandler, M.; Rose, F. Clifford. Dept. of Neurology, Charing Cross Hospital Medical School, London W6 8RF, England **The specific activity of platelet monoamine oxidase varies with platelet count during severe exercise and noradrenaline infusion.** Psychopharmacology. 72(3):275-277, 1981.

The effects of noradrenergic stimulation on platelet count and platelet monoamine oxidase (MAO) activity were studied in healthy male volunteers. Platelet count rose and then fell during severe exercise or noradrenaline infusion. Platelet MAO activity per unit protein rose and fell in parallel, and the correlation with platelet count was highly significant. The increase in specific MAO activity may be due to the release of a population of platelets with higher specific activity and the subsequent decrease in MAO activity may be due to their removal. 22 references. (Author abstract modified)

004510 Gloveli, T. B. Institut fiziologii im. I. S. Beritashvili, AN GruzSSR, Tbilisi, USSR **/The role of reticuloseptal inputs in the formation of different types of sensory reactions of the hippocampal neurons./** Rol' retikulo-septal'nogo vkhoda v formirovanii raznykh tipov sensornykh reaktsiy neyronov gippokampa. Soobshcheniya Akademii Nauk Gruzinskoy SSR. 100(3):661-664, 1980.

The role of reticulo septal inputs in the formation of various types of sensory reactions of the hippocampal neurons was studied in unanesthetized immobilized cats. The interruption of reticulo septal input by means of electrocoagulation of the medial septal nuclei, as well as by the intravenous injection of chlorpromazine, caused a depression of hippocampal electrical activity (theta-rhythm) and tonic reactions of single neurons. Unlike the effect of electrocoagulation of the medial septal nuclei, intravenous chlorpromazine also caused considerable reduction of spontaneous activity and complete depression of specific neural reactions. Thus, chlorpromazine is thought to have a direct influence on other brain structures, including the hippocampus. 15 references. (Journal abstract modified)

004511 Hanin, I.; Mallinger, A. G.; Kopp, U.; Himmelhoch, J. M.; Neil, J. F. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Mechanism of lithium-included elevation in red blood cell choline content: an in vitro analysis.** Communications in Psychopharmacology. 4(5):345-355, 1980.

The mechanisms of lithium induced elevation in red blood cell choline (Ch) content were investigated in vitro using gas chromatographic mass spectrometry combined with stable isotope methodology. The influx of deuterated Ch, and simultaneous efflux of endogenous Ch were measured in washed red blood cells incubated in vitro, and the influence of various parameters on these fluxes was investigated. The effect of lithium on red blood cell Ch levels is gradual, and ultimately irreversible. Its primary site of action appears to be at the level of red blood cell membrane, via inhibition of Ch transport both into and out of the red blood cell. The elevation in red blood cell Ch of patients chronically treated with lithium may result from a continuous breakdown of membrane phospholipids to release free Ch, and a concurrent irreversible inhibition of efflux of the accumulated Ch. The potential significance of these findings is discussed. 42 references. (Author abstract modified)

004512 Herning, R. I.; Rosenbaum, R.; Jones, R. T. Langley Porter Neuropsychiatric Institute, University of California Medical Center, San Francisco, CA **Event-related potential changes with morphine in non-addicted humans.** In: Barber, C., Evoked potentials. Baltimore, MD, University Park Press, 1980. 614 p. (p. 531-534).

To determine whether opiates may have effects on cognitive, event-related potential components and the contingent negative variation (CNV), rather than on primary sensory components, 17 subjects with no history of illicit opiate use, no recent medical opiate use, and minimal other drug use participated in a 2 day experiment. On one day they received an injection of morphine sulphate and on the other day they received a saline injection. At least 1 day intervened between the 2 test days. Both the P300 and CNV effect occurred at 30 minutes after the morphine injection and no changes were seen thereafter. The effect of morphine on pupil diameter and subjective reports peaked at 60 and 90 minutes. It would appear that many psychoactive, abused drugs reduce the P300. The correlates of whatever processes the P300 represents may be what the drug user seeks to decrease. The increased CNV following 0.14mg/kg of morphine in subjects who have abnormal MMPI profiles requires further systematic study. 6 references.

004513 Herrick, C. E.; Harding, G. F. A. Neuropsychology Unit, Ophthalmic Optics Dept., University of Aston, Birmingham, England **The effect of sodium valproate on the photosensitive VEP.** In: Barber, C., Evoked potentials. Baltimore, MD, University Park Press, 1980. 614 p. (p. 539-547).

Two experiments were conducted to determine the effect of stimulus parameters on the photosensitive visual evoked potential (VEP) and whether the therapeutic value of sodium valproate on general convulsive responses similarly affected this evoked potential. Sodium valproate has been found to improve significantly generalized spontaneous and photically induced abnormalities, while localized, occipital abnormality was found to be particularly resistant to treatment. It is proposed that sodium valproate operates on nonspecific visual pathways other than the specific primary projection. 41 references.

004514 Hollister, L. E.; Jenden, D. J.; DoAmaral, J. R.; Barchas, J. D.; Davis, K. L.; Berger, P. A. V.A. Hospital, 3801 Miranda Ave., Palo Alto, CA 94304 **Pharmacokinetic studies with choline chloride: a preliminary report.** In: Davis, K., Brain acetylcholine and neuropsychiatric disease. New York, Plenum Press, 1979. (p. 533-539).

An attempt was made to determine the dosage of choline chloride that produced the highest sustained plasma choline concentration in a series of acute and chronic studies. Nine patients received an oral dose of 5g of choline chloride daily in one study. In the other study, eight patients received initially 1g of choline chloride four times per day for a total of a 4g per day increment, every 3 days. The results indicate that the oral administration of choline chloride increases plasma choline levels in a dose dependent manner. Data from single dose studies suggest that plasma choline levels do not start to fall off until 6 hours after administration. This offers a rationale for giving choline chloride in four oral doses. After chronic treatment, plasma choline levels diminished much more gradually than after the acute ingestion. Thus, it is suggested that after a period of treatment longer intervals between choline chloride doses might be possible, and a sustained elevation in plasma choline maintained. 20 references.

004515 Howard-Peebles, Patricia N.; Pryor, Johnny C. Institute of Genetics/Dept. of Microbiology, University of Southern Mississippi, Hattiesburg, MS 39401 **Fragile sites in human chromosomes I. The effect of methionine on the Xq fragile site.** Research Report, NIMH Grant 1R03-MH-33321, 1980. 15 p.

The Xq-fragile site found in males having nonspecific X-linked mental retardation was studied by varying the chemical and physical parameters of leukocyte cultures. Methionine was shown to be required for marker expression in both medium 199 and MEM. Banding studies indicated that methionine does not function as a stabilizing factor for the fragile site on Xq. 17 references. (Author abstract)

004516 Humpel, Michael; Nieuweboer, Bob; Milius, Waltraud; Hanke, Heidrun; Wendt, Hans. Dept. Biodynamik, Schering AG, Mullerstrasse 170-178, D-1000 Berlin 65, West Germany **Kinetics and biotransformation of lormetazepam: II. Radioimmunologic determinations in plasma and urine of young and elderly subjects: first-pass effect.** Clinical Pharmacology and Therapeutics. 28(5):673-679, 1980.

The kinetics and biotransformation of a new benzodiazepine, lormetazepam, were investigated in young and elderly human Ss using a newly developed specific and sensitive radioimmunoassay. After intravenous injection, lormetazepam levels in plasma fell in three (alpha, beta, and gamma) dispositional phases, two of them (alpha, beta) mainly reflecting different distribution processes. The terminal (gamma) phase correlated well with the rate of renal elimination of glucuronides. Oral doses were completely absorbed with widely varying absorption half-lives amounting to an average of 0.67 hours. Dose dependent maximum plasma levels were reached in about 2 hours. Lormetazepam undergoes first pass metabolism of about 20% of an oral dose. Total clearance was in the range of 20ml/minute. There was a trend toward slower terminal disposition phase in elderly Ss. In younger Ss, the terminal phase absorption half-life was about 10 hours. Lormetazepam glucuronide peak plasma levels were reached by about 6 hours. Thereafter, the level fell in one (elimination) phase, with absorption half-life of 12 hours in young Ss and with a significantly different absorption half-life of

20 hours in the elderly Ss. Renal clearance was calculated as about 30 ml to 40 ml and did not show an age dependent difference. Recovery of lormetazepam glucuronide with urine amounted to 70% to 80% of the dose during 72 hours after intravenous injection in both age groups. 25 refernces. (Author abstract modified)

004517 Inotsume, Nobuo; Nakano, Masahiro. Pharmaceutical Division, Sumitomo Chemical Co., Osaka, Japan **Reversible ring-opening reactions of nimetazepam and nitrazepam in acidic media at body temperature.** Journal of Pharmaceutical Sciences. 69(11):1331-1334, 1980.

Hydrolytic reactions of nimetazepam and nitrazepam in acidic solution at body temperature were studied spectrophotometrically. The open ring compounds produced by hydrolysis were in equilibrium with the corresponding closed ring compounds (protonated nimetazepam and nitrazepam). Forward reaction rate constants of both drugs were greater than the rate constant of diazepam. In nimetazepam, the forward reaction rate constant was smaller than the reverse reaction rate constant; in nitrazepam, the reverse reaction rate constant was much smaller than the forward reaction rate constant, and possible amide bond cleavage was indicated. The activation energies of the forward and reverse reactions of nimetazepam and the forward reaction of nitrazepam were calculated from Arrhenius type plots, whereas no clear temperture dependency was observed in the reverse reaction rate constant of nitrazepam. The effect of Ph on these reactions also was examined. In addition the pKa values of nimetazepam and nitrazepam were calculated to be 2.53 and 2.77, respectively. 11 references. (Author abstract)

004518 Ishigooka, Jun; Tanaka, Kunio; Suzuki, Yasuyo; Katori, Makoto; Miura, Sadanori. Dept. of Psychiatry, Kitasato University School of Medicine, 1-15-1 Kitasato, Sagamihara 228, Kanagawa, Japan **Selective inhibitory effects of chlorpromazine and imipramine on platelet aggregation.** International Pharmacopsychiatry. 15(5):270-280, 1980.

The effects of chlorpromazine (CPZ) and imipramine (IMP) on platelet aggregation in vitro were investigated. Both CPZ and IMP inhibited epinephrine induced secondary aggregation in a dose dependent fashion and changed adenosine diphosphate (ADP) induced irreversible aggregation into a reversible response in human platelets. With rabbit platelets, CPZ (0.6 to 20mcM) and IMP (60 to 60mcM) showed a selective inhibitory effect on the aggregation by collagen, whereas, even at 200mcM, this effect was found neither in arachidonic acid (AA) induced aggregation nor in an ADP induced one. CPZ and IMP also inhibited human platelet aggregations induced by collagen, but not by AA. The antiaggregating action of CPZ and IMP was thought to be due to their inhibitory effects of AA liberation from platelet membranes, suggesting that they might inhibit participating enzymes (phospholipase A2, C, or lipase) or the process of the activation of the enzymes. 20 references. (Author abstract)

004519 Itil, Turan M.; Soldatos, Constantin; Bozak, M.; Ramadanoglu, Emel; Dayican, Gulay; Morgan, V.; Menon, G. N. Division of Biological Psychiatry, N.Y. Medical College, New York, NY **CNS effects of ISF-2522, a new nootropic (a phase I safety and CNS efficacy study with quantitative pharmaco-EEG and pharmaco-psychology).** Current Therapeutic Research. 26(5):525-538, 1979.

The CNS effects of ISF-2522, a new nootropic, were investigated. A single rising dose tolerance study in humans indicated that this compound is safe up to 2400mg as a single dose. Quantitative pharmaco EEG data demonstrated significant CNS effects of ISF-2522 in humans as determined by the discrimination from placebo and by the linear time dose related effects. Computer data base has classified ISF-2522 as a psychostimulant, similar to dextroamphetamine and piracetam. Because of the similarities of the CNS effects with piracetam, psychostimulant nootropic properties of ISF-2522 were predicted. The CNS effective daily dose of ISF-2522 was estimated as 1200 to 2400mg. 25 references. (Author abstract modified)

004520 Jenden, D. J.; Jope, R. S.; Fraser, S. L. Dept. of Pharmacology, University of California, School of Medicine, Los Angeles, CA 90024 **A mechanism for the accumulation of choline in erythrocytes during treatment with lithium.** Communications in Psychopharmacology. 4(5):339-344, 1980.

The kinetics of isotopic exchange of choline (Ch) between erythrocytes and the medium in which they are suspended were examined during a 4 hour incubation at 37 degrees C using (2H4)Ch in the medium at a concentration similar to that in plasma. (2H4)Ch and (2HO)Ch in erythrocytes and medium were measured by gas chromatography mass spectrometry. A steady-state was experimentally verified. The kinetics of exchange closely obeyed a simple model from which it is possible to estimate influx and efflux of Ch in three normal human Ss. In all Ss there was a substantial net efflux of Ch, representing Ch released from phospholipids within the cells. It is proposed that the rise in erythrocyte Ch levels during treatment with lithium is due to the inability of Ch to escape as fast as it is released when the transport system is inhibited by lithium. 10 references. (Author abstract modified)

004521 Jope, Richard S.; Jenden, Donald J.; Ehrlich, Barbara E.; Diamond, Jared M.; Gosenfeld, Lawrence F. Dept. of Pharmacology, School of Medicine, University of California, Los Angeles, CA 90024 **Erythrocyte choline concentrations are elevated in manic patients.** Proceedings of the National Academy of Sciences of the United States. 77(10):38-41, 1980.

Observations that changes in the metabolism and membrane transport of choline may be important in certain neuropsychiatric diseases were investigated. It was found that the intracellular choline concentration in erythrocytes of manic patients who never had lithium therapy was three times the value for normal human Ss. Lithium therapy increased this value to 11 times normal, and the increase began within the first 2 days of lithium therapy. Plasma choline concentration was normal in untreated manic patients and did not change during lithium therapy. 14 references. (Author abstract modified)

004522 Kapetanovic, Izet M.; Kupferberg, Harvey J.; Porter, Roger J.; Theodore, William; Schulman, Elliott; Penry, J. Kiffin. Kupferberg: Epilepsy Branch, Bldg. 36, Rm. 5D-21, NIH, Bethesda, MD 20205 **Mechanism of valproate-phenobarbital interaction in epileptic patients.** Clinical Pharmacology and Therapeutics. 29(4):480-486, 1981.

The effects of valproate on the biodisposition of phenobarbital were examined. In epileptic patients on a phenobarbital regimen, the addition of valproate led to elevated plasma phenobarbital levels and increased urinary output of unchanged phenobarbital. There was no effect on urinary pH. The increase in plasma phenobarbital was paralleled by a prolonged phenobarbital elimination half-life, and the decrease in plasma phenobarbital clearance was paralleled by a decrease in phenobarbital elimination rate constant. Results suggest that valproate elevates plasma phenobarbital level by inhibiting phenobarbital metabolism. 15 references. (Author abstract modified)

004523 Killian, Grant Aram. University of Chicago **The effects of psychotropic medication on cognitive control measures. (Ph.D.**

dissertation). Dissertation Abstracts International. 42(1):377-B, 1981. (Not available from Univ. Microfilms), 1981.

To investigate the effects of psychotropic medication on cognitive control measures, a battery of cognitive control measures were administered to 34 schizophrenic and 26 depressed, nonmedicated inpatients after a drug free period. These experimental groups were then given appropriate psychotropic medication and 4 weeks later were retested for a second time. Results were compared with those for drug free normals and medicated schizophrenics and depressed inpatients. No significant differences were found as a function of the drug condition on cognitive control measures. Although all groups showed some improvement on all the individual cognitive measures, neither of the two experimental groups improved more than the comparison groups. Overall, depressed patients changed the most, schizophrenic patients changed the least, and normal subjects were in between. It is concluded that cognitive control measures in schizophrenia and depression seem recalcitrant to available psychotropic agents. (Journal abstract modified)

004524 Klotz, U.; Kangas, L.; Kanto, J. Dr. Margarete-Fischer-Bosch-Institut fur Klinische Pharmakologie, Auerbachstr. 112, D-7000 Stuttgart 50, West Germany **Clinical pharmacokinetics of benzodiazepines.** Progress in Pharmacology. 3(3):1-72, 1980.

Pharmacokinetic characteristics of clinically useful benzodiazepines are reviewed. Chlordiazepoxide, diazepam, desmethyldiazepam/clorazepate, oxazepam, lorazepam, medazepam, clonazepam, flunitrazepam, flurazepam, and nitrazepam are extensively metabolized, including dealkylation, hydroxylation, reduction, and conjugation reactions. With the exception of oxazepam and lorazepam, the metabolites are biologically active and will accumulate during multiple dosing with the parent drug. Absorption after oral administration is rapid and almost complete. With the exception of flurazepam, these drugs are highly bound to plasma proteins. Disposition can be impaired in elderly patients and in patients with liver disease. 471 references. (Author abstract modified)

004525 Klotz, U.; Schweizer, C. Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Auerbachstr. 112, D-7000 Stuttgart 50, West Germany **Valproic acid in childhood epilepsy: anticonvulsive efficacy in relation to its plasma levels.** International Journal of Clinical Pharmacology, Therapy and Toxicology. 18(10):461-465, 1980.

Plasma levels of valproic acid were monitored for 2 years in 90 epileptic children. Of 34 patients treated with sodium valproate alone, complete seizure control was achieved in 82% with a mean plasma level of 65.1mcg/ml; the 6 patients whose seizures recurred appeared to be resistant to sodium valproate therapy, since their plasma levels were significantly higher (91.7mcg/ml) than those of the controlled patients. Of 14 children treated with valproate and phenobarbital, seizures were completely controlled in 64% with plasma levels of 54.6mcg/ml; valproate concentrations were lower (33.8mcg/ml) in the uncontrolled patients. Of 20 children treated with more than two anticonvulsants, complete seizure control was achieved in only 35%, with valproate plasma concentrations of 63.1mcg/ml. These findings suggest that 40 to 90mcg/ml may be an appropriate therapeutic range for sodium valproate. 16 references. (Author abstract modified)

004526 Krupenina, L. B.; Vinogradov, M. V. Lab. biokhimii i otdel psikhofarmakologii, Moskovskiy NII psikhiatrii, Ministerstvo zdravookhraneniya RSFSR, Moskva, USSR **/The state of the adrenergic and cholinergic systems in schizophrenic patients during psychpharmacotherapy./** Sostoyaniye adrenergicheskoy i kholinergicheskoy sistem u bol'nykh shizofreniyey v protsesse psikhofarmakoterapii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(5):737-745, 1980.

The state of catecholamine and acetylcholine metabolism in patients with recurrent, progressive attack like, and continuous forms of schizophrenia was studied during treatment with neuroleptics, and also in a control group. Dosages, duration of administration, and the course of the mental state were taken into consideration. In the schizophrenic Ss this system was different from that of the normal Ss; there was a correlation between the type of changes in catecholamine metabolism and the form of schizophrenia, prior to and during pharmacotherapy. 20 references. (Journal abstract modified)

004527 Kukwa, L. Ringstr. 13, D-8130 Starnberg, West Germany **/Pharmacological peculiarities of a benzodiazepine/ataractic drug and its therapeutic relevance: the special status of clorazepate dipotassium (Tranxilium)./** Pharmakologische Besonderheiten eines Benzodiazepin-Ataraktikums und deren therapeutische Relevanz: die Sonderstellung von Dikaliumclorazepat. Psycho: Neurologie und Psychiatrie fur die Praxis. 6(1):20,22,24,26-27, 1980.

The ataractic drug clorazepate dipotassium was examined for its therapeutic qualities. It caused a rapid and complete hydrolytic change in the stomach and intestines into N-desmethyldiazepam, a potent anxiolytic drug. Metabolic changes occurred under normal physiological conditions in the stomach and intestines. It is concluded that clorazepate dipotassium is a very useful drug for treating psychovegetative disturbances; it has few side-effects. It can be recommended for all psychic disturbances, but in particular it assures sound sleep and elevates the general mood. 14 references.

004528 Kuznetsova, V. I. Lab. patologicheskoy anatomiya TsNS, Moskovskiy NII psikhiatrii, Ministerstvo zdravookhraneniya RSFSR, Moskva, USSR **/Peculiarities of the cerebral pathomorphology of patients with schizophrenia treated with psychotropic drugs (pharmacological pathomorphosis)./** Osobennosti patomorfologii golovnogo mozga bol'nykh shizofreniyey lechennykh psikhotropnymi preparatami (k voprosu o lekarstvennom patomorfoze). Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(7):929-933, 1979.

Peculiarities of the pathomorphology of the brain of patients with schizophrenia who had been treated with psychotropic drugs were studied histologically. Results show that the use of psychopharmaceuticals to treat schizophrenic patients does not remove the characteristic neuronal pathology (shrinkage, atrophy, lipofuscin dystrophy, and cytolysis), but increases the metabolic processes in the intact nervous cells (increases the volume and basophilia in the cytoplasm, and enlarges the nuclei and nucleoli) and increases the glial activity (increases the amount of perineuronal satellites, general glia, and the glioneuronal index). 17 references. (Journal abstract modified)

004529 Lacko, L.; Wittke, B.; Lacko, I. Gustav-Embden-Zentrum der biologischen Chemie, Theodor-Stein-Kai 7, D-6000 Frankfurt/Main 70, West Germany **Interaction of chlorpromazine with the transport system of glucose in human erythrocytes.** Arzneimittel-Forschung. 30(11):1852-1855, 1980.

Characteristics of inhibition of the glucose uptake in human erythrocytes by chlorpromazine (CPZ) were investigated. It was found that CPZ is a strong inhibitor of glucose uptake in erythrocytes. The inhibition kinetics indicated that two molecules of CPZ can bind to the transport system and thus form two different CPZ complexes. The dissociation constants of both the CPZ complexes and the pH dependence and temperature dependence of the inhibition are described. 21 references. (Author abstract modified)

004530 Lavene, D.; Abriol, C.; Guerret, M.; Kiechel, J. R.; Lallemand, A.; Rulliere, R. Laboratoires Sandoz, 14, bd. Richelieu, F-92505 Rueil-Malmaison, France **/Pharmacokinetics of cloxazolam in man after single and multiple oral doses./** Etude pharmacocinetique du cloxazolam apres administration a dose unique et iterative chez l'homme. Therapie. 35(4):533-543, 1980.

The pharmacokinetics of cloxazolam, a 1,4 benzodiazepine anxiolytic, were studied. Seven subjects received a single 2mg and multiple (3 x 1mg daily) oral doses of cloxazolam for 9 days. Since after oral administration no measurable amounts of unchanged drug could be found in plasma, assays were performed on chloro-N-demethyl diazepam (CND), the main metabolite. CND in plasma samples was determined by electron capture gas liquid chromatography. After a single dose, CND was found in plasma only after a mean lag time of .9 hour and reached peak levels within 3 hours. Then CND was eliminated with an apparent biexponential pattern. In multiple dosage regimen, the plasma levels were determined the 6th, 8th, 9th days after initiation of therapy. The steady-state was almost reached after 8 days. There was a good correlation with a statistical significance between the observed plasma levels at steady-state with the predicted values, based on single dose parameters which indicated that the pharmacokinetics is linear, nonsaturable, reproducible from dosage to dosage and that chronic cloxazolam exposure has no apparent effect on its own metabolizing enzymes. 12 references. (Journal abstract modified)

004531 Lefebvre, J. Service d'Endocrinologie et Diabetologie, Universite de Lille, Rue du Professeur Laguesse 6, F-59037 Lille, France **Treatment of undernutrition and electrolyte disturbances in anorexia nervosa.** Acta Psychiatrica Belgica. 80(4):551-556, 1980.

Treatment of undernutrition and electrolyte disturbances in cases of anorexia nervosa is discussed. Treatment varies according to the amount of weight that has been lost, and depends on a precise evaluation of biological data, especially of electrolytes. Hypochloremie/hypokaliemic alcalosis is frequent and must be treated by isotonic saline perfusions until the plasma electrolytes return to normal. There are three methods of refeeding: oral, parenteral, and nasogastric tube feeding. The last method appears to be the most successful. Short-term treatment for slight undernutrition usually has good results. Long-term treatment for more serious cases, however, must be accompanied by psychological treatment. (Journal abstract modified)

004532 Lenehan, T.; Omer, L. M. O.; Darragh, A. Omer: F. Hoffman-La Roche & Co. Ltd., Dept. of Clinical Research and Development, Basle, Switzerland **Effects of Ro 11-2465, a new psychotropic agent on the uptake of serotonin by human platelets – in vitro determination of the IC50.** Archives Internationales de Pharmacodynamie et de Therapie. 249(1):147-152, 1981.

The effect of Ro-11-2465, a new psychotropic agent, on in vitro uptake of 3H-serotonin into human blood platelets was compared with the effects of commonly used antidepressants. The compounds inhibited serotonin uptake in a dose dependent manner. Ro-11-2465 was 6 times more potent than clomipramine and 14 times more potent than imipramine. Results suggest that Ro-11-2465 may have antidepressant properties. 11 references. (Author abstract modified)

004533 Loeb, C.; Roccatagliata, G.; Besio, G. Istituto di clinica neurologica, Universita di Genova, Via A. de Toni 5, I-16132 Genova, Italy **/Variations in urinary levels of 3-methoxy-4-hydroxyphenylglycol sulfate in patients with depressive syndromes./** Variazioni del livello urinario dell'MHPG nelle sindromi depressive. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie. 125(2):337-348, 1979.

Changes in urinary levels of 3-methoxy-4-hydroxyphenylglycol (MHPG) in a group of patients affected by different forms of depressive illness were studied. No significant differences were noted related to age, diagnosis, or number and duration of episodes. Considering the group as a whole, a significant increase in MHPG urinary levels was noted following recovery, although the patients received different drugs (tricyclic antidepressants plus phenothiazine, trazodone, and monoamine oxidase inhibitors, IMAO). Specifically, recovered or improved patients treated with trazodone or IMAO showed a remarkable increase in MHPG urinary levels, whereas a decrease was evidenced in the group that received tricyclic antidepressants. 42 references. (Journal abstract)

004534 Mardh, Goran; Sjoquist, Birgitta; Anggard, Erik. Dept. of Alcohol and Drug Addiction Research, Karolinska Institutet, S-104 01 Stockholm, Sweden **Norepinephrine metabolism in man using deuterium labelling: 4-hydroxy-3-methoxymandelic acid.** Journal of Neurochemistry. 36(3):1181-1185, 1981.

Plasmak and urine levels of 4-hydroxy-3-methoxyphenylglycol (HMPG) and 4-hydroxy-3-methoxymandelic acid (HMMA) were determined in five healthy men after i.v. pulse doses of 4.3mcmol HMPG labeled with deuterium. About 40% of the injected amount of labeled HMPG was recovered in the urine as HMMA. Another 40% was eliminated as HMPG conjugates. Results indicate that HMPG formed from norepinephrine in the central or peripheral nervous system undergoes both conjugation and extensive oxidation. 23 references. (Author abstract modified)

004535 Mazzi, C.; Riva, L. P.; Morandi, G.; Mainini, E.; Martinelli, I.; Bertaccini, G. Dept. of Endocrinology, St. Anthony Hospital, I-21013 Gallarate, Italy **Drug-induced alterations of the hypothalamus-hypophysis axis.** Acta Psychiatrica Belgica. 80(5):619-637, 1980.

The effects of acute administration of cimetidine, nomifensine, and domperidone on patterns of growth hormone (GH), prolactin (PRL), and thyroid stimulating hormone (TSH) were studied. Subjects were normal, were patients with pituitary nonsecreting and PRL secreting adenomas, or were patients with amenorrhea-galactorrhea syndrome without evidence of adenoma. Cimetidine increased PRL secretion and reduced both GH and TSH secretions in healthy subjects; in patients with nonsecreting adenoma the variations of GH and TSH levels were absent. Nomifensine inhibited PRL secretion in healthy subjects, an inhibition which did not appear in patients with nonsecreting adenoma or with PRL secreting adenoma. In healthy subjects, the GH level rose significantly following nomifensine administration, but a smaller response was seen in the other subjects. Domperidone administration had an inconstant action on PRL level and did not affect GH and TSH secretions. The results confirm the influence which drugs employed in the therapy of nonendocrine diseases have on the function of the hypothalamus. The possibility of analyzing CNS output through secretion of pituitary hormones is suggested. 21 references. (Author abstract modified)

004536 Mel'nichuk, P. V.; Minich, L. N. Klinika nervnykh bolezney, Moskovskiy meditsinskiy institut imeni I. M. Sechenova, Moskva, USSR **/Problems of treating deforming myodystonia with L-DOPA, and prediction of its therapeutic effect./** Voprosy lecheniya i prognozirovaniya terapevticheskogo effekta preparata L-DOFA pri deformiruyushchey myshechnoy distonii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(8):1002-1006, 1979.

Clinicobiochemical examinations were performed on 55 patients suffering from various forms of deforming myodystonia. L-DOPA was administered in 47 cases. A correlation between therapeutic effect and the level of phenylacetylglutamine excretion was observed. Positive results of treatment with L-DOPA were noted in 36 patients (77%) who also had increased levels of phenylacetylglutamine excretion. Resistance to the drug was observed in cases where phenylacetylglutamine excretion did not exceed normal levels. The quantitative determination of phenylacetylglutamine in the urine can be used as a prognostic test of the therapeutic efficacy of L-DOPA in patients with deforming myodystonia. 18 references. (Journal abstract modified)

004537 Mellerup, Erling T.; Dam, Henrik; Plenge, Per; Rafaelsen, Ole J. Psychochemistry Institute, Rigshospitalet, University of Copenhagen, 9 Blegdamsvej, DK-2100 Copenhagen O, Denmark **Lithium effects on citrate metabolism in humans and rats.** Psychopharmacology. 73(1):75-76, 1981.

The effects of lithium on citrate metabolism in long-term lithium treated patients and experimental animals were investigated. Lithium treatment of manic-depressive patients was accompanied by decreased blood citrate, whereas lithium to rats led to increased blood citrate levels. The implications of these findings for urinary calcium excretion in lithium treated humans and animals are discussed. The low urinary calcium in lithium treated patients and the high urinary calcium in lithium treated rats may, at least partly, be explained by the low and high blood citrate levels in each species. 19 references. (Author abstract modified)

004538 Meltzer, Herbert Y.; Busch, Daniel; Young, Michael; Tricou, Betty Jo; Nasr, Suhayl; Metz, John; Fang, Victor. Dept. of Psychiatry, Pritzker School of Medicine, University of Chicago, Chicago, IL 60615 **Prolactin and growth hormone studies in schizophrenic patients and normal controls.** In: Brambilla, F., ed., Progress in psychoneuroendocrinology. New York, Elsevier/North Holland, 1980. 669 p. (p. 283-294).

Prolactin (PRL) and growth hormone (GH) levels were studied in schizophrenic patients. Serum PRL levels were within normal limits in drug free chronic schizophrenic patients. Acute schizophrenics had slightly elevated PRL levels. The GH response to the dopamine agonist apomorphine was correlated with the duration of illness; apomorphine produced significantly smaller increases in GH in patients with longer duration of illness. Chronic L-DOPA administration diminished the GH response to apomorphine. The evidence suggests that the reduced GH response in schizophrenics may be the result of prolonged dopaminergic stimulation. Excessive dopaminergic stimulation also may account for the decreased PRL response to low doses of chlorpromazine in female chronic schizophrenics. 38 references.

004539 Merali, Z.; Lapierre, Y. D. University of Ottawa School of Medicine, 275 Nicholas St., Ottawa, Ontario K1N 9A9, Canada **Prolactin and neuroleptic drugs: a biochemical index of clinical response?** International Journal of Mental Health. 9(3-4):140-161, 1980/1981.

The relationship between serum prolactin levels and neuroleptic drugs is discussed. Neuroleptics have an inhibitory action on dopaminergic neurotransmission and thus mediate the disinhibition of prolactin secretion. Studies indicate that prolactin response is dose related. A clinical study is reported on the use of two neuroleptics, fluphenazine decanoate and pipothiazine palmitate, in 36 chronic schizophrenics. The results indicate that elevation of serum prolactin in response to pipothiazine was of a greater magnitude than that following administration of fluphenazine decanoate. Females were more sensitive to the neuroleptic induced disinhibition of prolactin release than were their male counterparts. In contrast to reports on short-acting neuroleptics, a ceiling effect on prolactin elevation was not observed when therapeutically effective dosages of long-acting preparations were used. An overall curvilinear relationship between symptoms and prolactin change was observed. The predicted negative relationship between clinical response and prolactin clearly was evident mainly in females on pipothiazine palmitate. 55 references. (Author abstract modified)

004540 Metz, John; Busch, Daniel A.; Meltzer, Herbert Y. Dept. of Psychiatry, University of Chicago, Chicago, IL 60637 **Des-tyrosine-gamma-endorphin: H-reflex response similar to neuroleptics.** Life Sciences. 28(18):2003-2008, 1981.

In a study of eight schizophrenic patients, des-tyrosine-gamma-endorphin was found to significantly reduce secondary facilitation of the H-reflex recovery curve. This result is similar to the effect found after treatment with classical neuroleptic medication. The effect is different from that produced by lithium carbonate or antidepressants. This suggests that des-tyrosine-gamma-endorphin and neuroleptics have a similar pharmacological action in man. 18 references. (Author abstract)

004541 Mitkevich, S. P.; Kolyaskina, G. I. Lab. obshchey patofiziologii, Institut psikhiatrii, AMN SSSR, Moskva, USSR /**The effect of chlorpromazine and mageptil on the proliferation of peripheral blood lymphocytes in cultivation with phytohemagglutinin.**/ Vliyaniye aminazina i mazheptila na proliferatsiyu limfotsitov perifericheskoy krovi v usloviyakh kul'tivirovaniya s fitogemagglyutininom. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(2):115-117, 1981.

The effect of chlorpromazine and mageptil on the proliferation of peripheral blood lymphocytes in cultivation with phytohemagglutinin was studied in healthy people. Peripheral blood lymphocytes were incubated with phytohemagglutinin (50mcg/ml), and with chlorpromazine or mageptil in the following concentrations: 0.001, 0.01, 0.1, 5, and 10mcg/ml. The following cultures were studied: lymphocytes with 20% autologous serum; lymphocytes with 20% autologous serum and phytohemagglutinin; and lymphocytes with 20% autologous serum, phytohemagglutinin, and chlorpromazine or mageptil. The cultures were incubated for 72 hours at a temperature of 37dgrees C entigrade. The rate of stimulation or inhibition of the lymphocytes was determined. Results show that chlorpromazine and mageptil, added in concentrations of 5mcg/ml, 10mcg/ml, respectively, inhibit the proliferation of phytohemagglutinin stimulated lymphocytes. 13 reference. (Journal abstract modified)

004542 Myllyla, V. V.; Heikkinen, E. R.; Hokkanen, E.; Vapaatalo, H. Dept. of Neurology, University of Oulu, SF-90220 Oulu 22, Finland **Cyclic nucleotides and the nervous system.** Progress in Pharmacology. 3(2):67-106, 1980.

The role of cyclic nucleotide in the nervous system is reviewed. Cyclic AMP and cyclic GMP are abundant in the mammalian brain and appear to have opposing influences on cellular function in most tissues studied. Cyclic nucleotides serve as intracellular mediators for many extracellular substances such as amine and polypeptide hormones that do not penetrate into cells. Cyclic AMP accumulation can be induced in animal brain by catecholamines, serotonin, histamine, anoxia, decapitation, electrical stimulation, trauma, and various drugs. Cyclic GMP appears to be associated with cholinergic, dopaminergic, and GABAergic transmission. Changes in cyclic nucleotide concentrations in extracellular space (plasma, CSF, and urine) may reflect alterations in brain metabolism. Epileptic attack, rapidly progressing CNS damage, severe acute cerebrovascular disorders, and tramatic brain injury are associated with increased cyclic AMP in human CSF. 86 references.

004543 Nikandrova, L. R. Institut gigiyeny truda i profzabolevaniy AMN SSSR, Moskva, USSR /**A comparative evaluation of the usefulness of psychophysiological tests during various levels of activation of the central nervous system.**/ Sravnitel'naya otsenka informativnosti psikhofiziologicheskikh testov pri raznykh urovnyakh aktivatsii tsentral'noy nervnoy sistemy. Gigiyena Truda i Professional'nyye Zabolevaniya. No. 7:29-33, 1980.

The usefulness of psychophysiological tests at various levels of activation of the CNS was studied comparatively in 14 tests on each of 12 male scientific workers (28 to 33 years old). Different levels of activation of the CNS were brought about by the administration of chlorpromazine in three different doses. Results show that a psychopharmacological model can be used to analyze comparatively the informative value of tests of mental work capability. These results indicate that, in order to evaluate the mental work capability of a given category of people, the most useful tests are tests of complex audiomotor reactions and long-term memory for figures. The usefulness of these tests increases with the load on those higher mental functions which are connected with productive thinking, and it depends on the adequacy of the test problem in relation to the structure of the mental activity. 14 references.

004544 Patterson, Terry; Venables, Peter H. Research Dept., Menninger Foundation, Box 829, Topeka, KS 66601 **Bilateral skin conductance and the pupillary light-dark reflex: manipulation by chlorpromazine, haloperidol, scopolamine, and placebo.** Psychopharmacology. 73(1):63-69, 1981.

The manipulation of bilateral skin conductance and the pupillary light/dark reflex by chlorpromazine, haloperidol, scopolamine, and placebo was investigated. Cholinergic blocking with scopolamine produces skin conductance orientating response (SCOR) nonresponding in normal Ss. This may be one of a number of causes for nonresponding in schizophrenic Ss. Blockade of dopamine with haloperidol produces an increase in amplitude and shortening of recovery time in the SCOR of normal Ss. This result closely resembles that of Nielsen and Peterson (1976) who found a similar pattern of responding in normal Ss who scored high on a scale of schizophrenism. These results, along with those for chlorpromazine and the pupillographic effects of the three drugs are discussed in terms of biochemical working hypotheses of schizophrenic subclassification. 20 references. (Author abstract modified)

004545 Paxton, James W.; Donald, Roger A. Dept. of Pharmacology and Clinical Pharmacology, University of Auckland School of Medicine, Private Bag, Auckland, New Zealand **Concentrations and kinetics of carbamazepine in whole saliva, parotid saliva, serum ultrafiltrate, and serum.** Clinical Pharmacology and Therapeutics. 28(5):695-702, 1980.

Concentrations and kinetics of carbamazepine in whole saliva, parotid saliva, serum ultrafiltrate, and serum were investigated in six healthy Ss. Ss received a 400mg oral dose of carbamazepine (CBZ). CBZ concentrations were determined by enzyme immunoassay in whole saliva, serum, and serum ultrafiltrate over 82 hours. After 30 hours, the log concentration time plots declined linearly with similar elimination half-lifes in all three fluids. Although the mean ultrafiltrate curve was lower than the mean salivary curve, the area under the curve, volume of distribution, and total body clearance calculated from whole saliva and ultrafiltrate data were not different. The mean CBZ concentration ratios of whole saliva/total serum and ultrafiltrate/total serum of the individual Ss ranged from 19.6% to 34.7% and from 19.0% to 28.8%. Linear correlations were found between salivary CBZ concentrations and serum and ultrafiltrate concentrations. Whole salivary and uncontaminated parotid salivary CBZ concentrations were not different and were independent of volume of fluid produced, pH of saliva, and degree of stimulation. Results indicate that whole saliva may be a suitable medium for monitoring free concentrations of CBZ and may provide a noninvasive alternative to blood. 12 references. (Author abstract modified)

004546 Puzynski, Stanislaw; Bidzinski, Andrzej; Zaluska, Maria. Instytut Psychoneurologiczny, Al. Sobieskiego 1/9, 02-957 Warszawa, Poland /**The activity of erythrocyte catechol-o-methyltransferase in endogenous depressive syndromes.**/ Aktywnosc katechol-o-metylotransferazy erytrocytow w endogennych zespolach depresyjnych. Psychiatria Polska. 14(6):569-573, 1980.

The activity of catechol-o-methyltransferase (COMT) was examined in the erythrocytes of 31 normal individuals (16 men, 15 women) and 24 patients with endogenous depressive syndrome (7 men, 17 women). It was found that the activity of the enzyme was statistically significantly increased in women with endogenous depressive syndromes in comparison with normal women. No correlation was found between the activity of the enzyme and the intensity of axial depressive symptoms, nor did pharmacotherapy with amitriptyline or mianserin exert any significant influence on the activity of COMT. 15 references. (Journal abstract modified)

004547 Puzynski, Stanislaw; Hauptmann, Miroslawa; Zaluska, Maria. Instytut Psychoneurologiczny, Al. Sobieskiego 1/9, 02-957 Warszawa, Poland /**The activity of blood platelet monoamine oxidase in endogenous depression.**/ Aktywnosc MAO w plytkach osob z endogennym zespolem depresyjnym. Psychiatria Polska. 14(6):575-580, 1980.

The activity of blood platelet monoamine oxidase (MAO) was examined in 31 normal subjects (15 men, 16 women) and in 24 patients with endogenous depression (7 men, 17 women). The activity of the enzyme showed a statistically significant higher level in healthy women than in healthy men, and was significantly lower in an undifferentiated group of women with endogenous depression, particularly in women with bipolar affective illness. It was found that there was a correlation between the activity of the enzyme and the measure of disturbances in biological rhythms (r=0.533). An increase in monoamine oxidase activity was observed after a week of treatment with uniform dosages of amitriptyline or mianserin. In addition, during the clinical stage of improvement or remission of depressive symptoms, the activity of monoamine oxidase showed a statistically insignificant increase in comparison with the pretreatment activity of the enzyme. 22 references. (Journal abstract modified)

004548 Puzynski, Stanislaw; Rode, Anna; Zaluska, Maria. Instytut Psychoneurologiczny, Al. Sobieskiego 1/9, 02-957 Warszawa, Poland /**The activity of dopamine beta-hydroxylase in the plasma of patients with endogenous depressive syndromes.**/ Aktywnosc beta-hydroksylazy dopaminy w osoczu chorych z endogennymi zespolami depresyjnymi. Psychiatria Polska. 14(6):581-586, 1980.

A group of 26 patients with endogenous depressive syndromes (18 women and 8 men) ranging in age from 27 to 63 years were examined. Dopamine beta-hydroxylase (DBH) was measured before the beginning of treatment, during treatment with amitriptyline or mianserin, and in the period of improvement or total remission. A control group consisted of 30 healthy individuals ranging in age from 23 to 65 years (15 women and 15 men). The sex factor was found not to influence DBH activity either in the control group or in the group of patients with endogenous depression. Neither were there any statistically significant differences in the mean level of the enzyme between the group of healthy individuals and the group of patients with endogenous depression, nor between the nosologically differentiated subgroups of depressive patients. The antidepressant drugs used in therapy (amitriptyline and mianserin) had no significant influence on the initial DBH activity in the group of patients with endogenous depressive syndromes. 14 references. (Journal abstract modified)

004549 Rey, Alix C.; Buchsbaum, Monte S.; Post, Robert M. Section on Psychopharmacology, Maryland Psychiatric Research Center, Baltimore, MD **Apomorphine, haloperidol and the average evoked potentials in normal human volunteers.** Communications in Psychopharmacology. 4(4):327-334, 1980.

Somatosensory and visual evoked potentials were recorded in 15 normal volunteers given single doses of either apomorphine, haloperidol, or saline placebo on three separate days. Apomorphine and haloperidol reduced evoked potential amplitude for both somatosensory and visual systems. The evoked potential latency in the somatosensory system was significantly shortened by apomorphine and lengthened by haloperidol; similar trends were seen for visual evoked potentials. These results with dopamine agonists and antagonists suggest the sensitivity of evoked potentials either for the assessment of dopamine mechanisms or for some secondary effect of these drugs, such as one on the endorphin system. 26 references. (Author abstract modified)

004550 Rudorfer, Matthew V.; Young, Robert C. Young: New York Hospital/Cornell Medical Center, Westchester Division, 21 Bloomingdale Road, White Plains, NY 10605 **Anticholinergic effects and plasma desipramine levels.** Clinical Pharmacology and Therapeutics. 28(5):703-706, 1980.

Anticholinergic effects of the tricyclic antidepressant desipramine were studied in 12 outpatients. Salivation and pulse rate and subjective ratings of mouth dryness and palpitations were assessed before and during treatment with desipramine at a final daily dosage of 150mg. There were significant changes after 3 weeks of treatment in all parameters except ratings of palpitation. Ss with moderate or high plasma desipramine levels had more suppression of salivation than those with low levels. Changes in salivation and pulse did not correlate, nor did they correlate with subjective reports. 15 references. (Author abstract modified)

004551 Sasahara, Kunihiro; Nitanai, Takashi; Habara, Taeko; Morioka, Tadashi; Nakajima, Eiichi. Product Development Laboratories, Sankyo Company Ltd., 1-2-58, Hiromachi, Shinagawa, Tokyo, Japan **Dosage form design for improvement of bioavailability of levodopa III: influence of dose on pharmacokinetic behavior of levodopa in dogs and parkinsonian patients.** Journal of Pharmaceutical Sciences. 69(12):1374-1379, 1980.

The relationship between dose of levodopa and its pharmacokinetic behavior after i.v. and oral administration was investigated in dogs and in patients with Parkinson's disease. Six beagle dogs were given single i.v. doses of 2.4, 4.8, and 9.6mg/kg levodopa and single oral doses of 4.8, 9.6, and 19.2mg/kg in a crossover design. Three parkinsonian patients were given single oral doses of about 3.8, 7.7, and 15.4mg/kg levodopa. Plasma samples were analyzed for intact levodopa and total dopamine. The relationship between the area under the plasma concentration/time curve (AUC) of levodopa and the i.v. dose was linear in dogs. However, in both dogs and humans Ss, the relationship after oral doses was nonlinear, with the relative AUC increasing with increasing dose. 14 references. (Author abstract modified)

004552 Sellers, E. M.; Naranjo, C. A.; Giles, H. G.; Frecker, R. C.; Beeching, M. Addiction Research Foundation, 33 Russell St., Toronto, Ontario, M5S 2A1, Canada **Intravenous diazepam and oral ethanol interaction.** Clinical Pharmacology and Therapeutics. 28(5):638-645, 1980.

The mechanism of the interaction between ethanol and diazepam was investigated among six healthy male volunteer Ss. Ss were randomly assigned to each of two treatments: 1) diazepam (10mg i.v. over 20 minutes) preceded by 60 minutes with ethanol 0.7g/kg (diluted to 20%v/v) orally over 15 minutes and followed for 8 hours by ethanol 0.15g/kg to maintain the blood alcohol concentrations between 800 and 1,000mg/l; and 2) diazepam 10mg i.v. over 20 minutes. The area under the curve (AUC) for total diazepam increased in all Ss after ethanol. Since AUC of free diazepam also rose in all Ss and AUC of the metabolite N-desmethyldiazepam fell, there had been inhibition of hepatic intrinsic clearance of free drug. The susceptibility of individuals to inhibition of N-desmethylation by ethanol is qualitatively determined by total drug concentrations. Estimation of free diazepam concentration coupled with measurement of metabolite affords a qualitative and quantitative evaluation of the mechanisms of this interaction. 20 references. (Author abstract modified)

004553 Sicuteri, F.; Anselmi, B.; Del Bianco, P. L. Dept. of Clinical Pharmacology, University of Florence, I-50134 Florence, Italy **Dopamine and 5-HT supersensitivity in nonorganic central pain and in morphine abstinence: fortuitous or real analogy?** Advances in Biochemical Psychopharmacology. 22:523-533, 1980.

The roles of dopamine (DA) and serotonin (5-hydroxytryptamine, 5-HT) in nonorganic central pain and in morphine abstinence were investigated. An impressive supersensitivity (up to 1000fold) to DA and 5-HT of the smooth muscle (hand dorsal vein) was detected both in central panalgesia sufferers and in addicts during spontaneous or pharmacological abstinence. A 5-HT and dopamine supersensitivity of lesser intensity (10fold to 30fold) was found during migraine attacks. On these occasions, morphine-like factors in cerebrospinal fluid appear reduced or undetectable, reinforcing the chemical analogy between morphine abstinence and migraine attacks. Evidence of opiate receptors in the human vein is discussed; 5-HT venospasms, inhibited by morphine, promptly emerged when naloxone was inoculated locally. 24 references.

004554 Simpson, Michael; Parrott, Eugene L. Parrott: Division of Pharmaceutics, College of Pharmacy, University of Iowa, Iowa City, IA 52242 **Oral and rectal absorption of chloral hydrate and its betaine complex.** Journal of Pharmaceutical Sciences. 69(2):227-228, 1980.

Chloral hydrate and its betaine complex were administered orally and rectally to healthy male Ss, and urinary excretion of its metabolite trichloroacetic acid was determined. No significant difference was found between absorption of chloral hydrate and its betaine complex. For both chloral hydrate and its betaine complex, absorption was greater after oral administration than after rectal administration. 14 references. (Author abstract modified)

004555 Smith, M. T.; Eadie, M. J.; Brophy, T. O'Rourke. Dept. of Medicine, University of Queensland, Royal Brisbane Hospital, Brisbane, Australia **The pharmacokinetics of midazolam in man.** European Journal of Clinical Pharmacology. 19(4):271-278, 1981.

The pharmacokinetics of midazolam, a new water soluble benzodiazepine, were studied among six volunteers who were administered midazolam 5mg iv, 10mg oral solution, or 10mg oral tablet. Midazolam plasma concentrations were measured using an electron capture gas liquied chromatographic assay. After 5mg intravenous midazolam, Ss fell asleep within 1 to 2 minutes and continued to sleep for an average of 1.33 hours. After oral midazolam intake (solution or tablets), drowsiness appeared after an average of 0.38 hours and sleep continued for an average of 1.17 hours. The time to reach peak plasma midazolam concentrations did not differ for the two oral forms. The first pass effect, F, determined experimentally, indicated the substantial first pass metabolism of midazolam. The percentage of the midazolam dose excreted unchanged in urine in four Ss during the 0 to 8 hour urine collection interval was very small. 5 references. (Author abstract modified)

004556 Snyder, Scott; Karacan, Ismet; Salis, Patricia J. Portsmouth Psychiatric Center, Portsmouth, VA **Disulfiram and nocturnal penile tumescence in the chronic alcoholic.** Biological Psychiatry. 16(4):399-406, 1981.

Placebo or disulfiram was administered to 30 male, sober alcoholic inpatients in a random double-blind design in order to evaluate the effects of disulfiram on nocturnal penile tumescence. The amount and frequency of full erections were decreased in the cohort receiving disulfiram. Implications of these results for the role of norepinephrine in penile tumescence are discussed. 25 references. (Author abstract)

004557 Stephens, R.; Green, J.; Haycook, W.; Kilgore, M. Green: 2550 Park St., Jacksonville, FL 32204 **Electroencephalographic change in parkinsonian patients treated with levodopa-carbidopa.** Clinical Electroencephalography. 10(1):31-34, 1979.

EEG changes were studied in 21 parkinsonian patients treated initially with levodopa alone and then switched to levodopa/carbidopa combination therapy. No significant improvement was observed during the combination therapy. A slight increase in basic background frequencies was associated with the combination therapy, but the change was not significant. 23 references.

004558 Warren, James W., Jr.; Benmaman, Joseph D.; Wannamaker, Braxton B.; Levy, Rene H. College of Pharmacy, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29403 **Kinetics of a carbamazepine-ethosuximide interaction.** Clinical Pharmacology and Therapeutics. 28(5):646-651, 1980.

The kinetics of a carbamazepine/ethosuximide interaction were investigated. Six normal Ss took one 250mg ethosuximide capsule twice each day for 55 consecutive doses (study days 1 to 28) and one 200mg carbamazepine tablet each evening from study days 11 to 27. Plasma samples were collected on study days 10, 17, 21, and 28. Mean steady-state concentrations of ethosuximide declined by 17% from a preinduction (study day 10) level of 32.2mcg/ml to a postinduction level of 26.8mcg/ml on study day 28. Ethosuximide clearance increased between study days 10 and 28 from 0.664 l/hour to 0.800 l/hour. The time course of induction was analyzed using a kinetic induction theory. Ethosuximide half-life was lowered from 53.7 hours (before induction) to 44.6 hours (after induction); the difference between some Ss was large. These data indicate that ethosuximide disposition is altered by carbamazepine. 18 references. (Author abstract modified)

004559 Wode-Helgodt, Birgitta; Alfredsson, Gunnel. Dept. of Psychiatry, St. Goran's Hospital, S112 81 Stockholm, Sweden **Concentrations of chlorpromazine and two of its active metabolites in plasma and cerebrospinal fluid of psychotic patients treated with fixed drug doses.** Psychopharmacology. 73(1):55-62, 1981.

Concentrations of chlorpromazine and two of its active metabolites in plasma and cerebrospinal fluid (CSF) of schizophrenic patients treated with fixed drug doses were investigated. There was a significant correlation between the area under curve (AUC) for chlorpromazine (CPZ) in serum during 24 hour treatment and serum concentration at different fixed times of the day. The half-life for CPZ was found to be 8 to 33 hours. 7-OH-CPZ and nor1-CPZ disappeared at about the same rate as the parent compound. The concentration of both metabolites was less than 10 ng/ml after 36 hours. The levels of CPZ and metabolites presented a weak positive correlation to daily dose but not to dose calculated by mg/kg bodyweight. Older patients tend to have higher CPZ and metabolite levels. The dose effects are very similar in plasma and CSF and there is a significant correlation between CPZ levels in serum and CSF. CSF/plasma ratio for CPZ seems to be an individual factor possibly related to variations in protein binding in plasma and CSF. 28 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

004560 Backwell, Barry; Peterson, George R.; Kuzma, Ronald J.; Hostetler, Russell M.; Adolphe, Allen B. Wright State University School of Medicine, Dayton, OH 45431 **The effect of five tricyclic antidepressants on salivary flow and mood in healthy volunteers.** Communications in Psychopharmacology. 4(4):255-261, 1980.

A double-blind, randomized, Latin-square design was used to study the effects of five tricyclic antidepressants on salivary flow and mood in 12 normal volunteers. Differences from baseline were measured 5 hours after administration of placebo or 100mg of drugs. Salivary flow was determined by change in weight of dental swabs placed in the mouth, and change in mood was determined by the Clyde Mood Scale. Analysis of variance revealed significant treatment effects for salivary flow and all six Clyde Mood factors. Amitriptyline produced most change in salivation and all Clyde Mood factors, followed by doxepine (salivation and four out of six clyde mood factors). Desipramine produced least change in salivation and all except one Clyde Mood factor. Imipramine and nortriptyline were intermediate and interchangeable in their effects. These results are consistent with those in a number of other studies in animals on a variety of central and peripheral tissues which show the widest separation in activity between amitriptyline and desipramine. The findings are discussed in relationship to structure/activity relationships, mechanism of action, and adverse effects of the tricyclic antidepressant drugs. 13 references. (Author abstract modified)

004561 Delwaide, P. J.; Devoitille, J. M.; Ylieff, M. Hopital de Baviere, University of Liege, Boulevard de la Constitution 66, B-4020 Liege, Belgium **Acute effect of drugs upon memory of patients with senile dementia.** Acta Psychiatrica Belgica. 80(5):748-754, 1980.

The effects of physostigmine, scopolamine, lysin-vasopressin, and piracetam on memory performance were investigated in senile demented patients. Subjects' memory performance was assessed using the Rey Auditory Verbal Learning Test. A decrease in memory performance was found with scopolamine which is attributed to a specific effect upon the cholinergic system involved in the memorization process. Piracetam improved memory in the Rey test, but the effect was transient and was followed by a reversed effect after 48 hours. Lysin-vasopressin significantly facilitated memorization. Results show no effect of physostigmine on memory performance. 14 references. (Author abstract modified)

004562 Denijs, E. L. Brink 4, NL-2211 BK Noordwijkerhout, The Netherlands **Clinical evaluation of bromperidol versus haloperidol in psychotic patients.** International Pharmacopsychiatry. 15(5):309-317, 1980.

The activity of bromperidol was compared to that of haloperidol, as an initial treatment on admission of psychotic patients. In general, patients reacted equally to both drugs, showing a marked improvement in most of the scored psychiatric elements. After 2 weeks, an improvement in the energy score was noticed for bromperidol, but not for haloperidol, which emphasizes the disinhibiting effect of bromperidol. Most frequent side-efects were tremor, parkinsonism, and acathisia. In view of the importance of more stimulating drugs favoring social reintegration of some chronic psychotics, it is suggested that long-term follow-up studies with oral bromperidol are indicated. 13 references. (Author abstract modified)

004563 Frowein, H. W. Centrale Directie der PTT, Afd. CASWO 1, Postbus 30000, NL-2500 GA Den Haag, The Netherlands **Selective effects of barbiturate and amphetamine on information processing and response execution.** Acta Psychologica. 47(2):105-115, 1981.

A group of 12 Ss carried out a choice reaction task with reaction time (RT) and movement time (MT) as response measures. Independent variables were drug treatment (amphetamine, barbiturate, placebo), visual stimulus degradation and S-R compatibility. Visual stimulus degradation and S-R compatibility showed additive effect on the RT but did not affect the MT. This confirms that stimulus encoding, response selection, and response execution represent independent processing stages. The two drugs had selective effects on the RT and the MT. Barbiturate had no effect on the MT but lengthened the RT, and this effect was additive with the effects of S-R compatibility but showed an interaction with the effects of stimulus degradation. Amphetamine shorted the MT, but had no significant main effect on the RT although interaction with the effect of S-R compatibility was significant. These results suggest that barbiturate affects stimulus encoding, whereas amphetamine affects response related processes. 27 references. (Author abstract modified)

004564 Gath, Isak; Bar-On, E.; Rogowski, Z.; Bental, E. Technicon-Israel Institute of Technology, Julius Silver Institute of Bio-Medical Engineering Sciences, Technicon City, Haifa 32,000, Israel **Computerized analysis of sleep recordings applied to drug evaluation: midazolam in normal subjects.** Clinical Pharmacology and Therapeutics. 2994):533-541, 1981.

Computer analysis of polygraphic sleep recordings was used to evaluate the effects of midazolam, a benzodiazepine hypnotic. Results revealed a slight intranight REM rebound during medication and a reduction of stage-4 sleep after withdrawal. The relative power of the delta frequency band did not alter during medication or withdrawal. 27 references. (Author abstract modified)

004565 Gershon, E. S.; Nurnberger, J. I.; Jimerson, D. C. Section on Psychogenetics, Biological Psychiatry Branch, NIMH, Bldg. 10, Rm. 3N218, 9000 Rockville Pike, Bethesda, MD 20205 **Sex, plasma prolactin and plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) predict heritable d-amphetamine excitation in man. (Unpublished paper).** Bethesda, MD, NIMH, 1980. 9 p.

Behavioral responses to 0.3mg/kg i.v. d-amphetamine were studied in 13 monozygotic twin pairs using a double-blind randomized crossover design of active drug and placebo injections. Two independent behavioral responses, termed excitation and elation, were concordant in twin pairs and were reproducible within individuals. Elation was correlated with plasma amphetamine levels, but excitation was not. Higher excitation was predicted by male sex, lower predrug plasma prolactin, and higher predrug total plasma MHPG. Growth hormone response after amphetamine was greater in persons with higher excitation scores. All of the biological measures, but predrug prolactin were concordant in twin pairs. These data may imply higher activity of norepinephrine and dopamine in persons with high excitation response. Neurochemical differences between the sexes were implied also. 29 references (Author abstract)

004566 Griffiths, Roland R.; Bigelow, George E.; Liebson, Ira; Kaliszak, Julia E. Psychiatry, 623 Traylor, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Drug preference in humans: double-blind choice comparison of pentobarbital, diazepam and placebo.** Journal of Pharmacology and Experimental Therapeutics. 215(3):649-661, 1980.

In a residential hospital research ward, the effects of and preference for placebo and various oral doses of pentobarbital and diazepam were studied in volunteer human Ss with documented histories of sedative abuse. Drug free days alternated with drug administration days throughout the study. In Experiment 1, pentobarbital produced dose related increases in S rated and observer rated drug effects, and Ss generally chose higher pentobarbital doses over lower doses. Diazepam produced only modest elevations in drug effect ratings, and Ss did not consistently choose higher doses over lower doses. 400mg of pentobarbital and 200mg of diazepam produced Ss drug effect ratings and observer drug effect ratings of similar magnitude while placebo produced negligible effects. All Ss chose pentobarbital over placebo and diazepam over placebo on all occasions. All Ss chose pentobarbital over diazepam on the majority of choice trials. 42 references. (Author abstract modified)

004567 Itil, Turan M.; Bozak, M.; Polvan, N.; Soldatos, C.; Shapiro, D. M.; Krynicki, V.; Morgan, V. Dept. of Psychiatry, New York Medical College, 150 White Plains Road, Tarrytown, NY **Effects of supidimide (CG-3033) on objective and subjective sleep parameters (a sleep laboratory study).** Current Therapeutic Research. 27(3):442-457, 1980.

The hypnotic effects of three dosage levels of supidimide (CG-3033), a compound related to thalidomide, were assessed in 10 insomniac adults in a double-blind sleep laboratory study. Placebo and flurazepam were control drugs. Active drugs did not statistically change the sleep stages, but they increased REM latency in comparison to placebo. Flurazepam and 200mg supidimide improved the quality of sleep as determined by subjective ratings. Computer analyzed EEG indicated that the mode of action supidimide is different from that of flurazepam. It is concluded that supidimide may have a potential value as a hypnotic which produces a sleep without any significant change in the structure of the all night sleep process as determined by EEG and REM measurements. In the dosages investigated in this study (up to 200mg), the sleep producing effects of supidimide were not associated with having hangover effects or ataxia. 33 references. (Author abstract)

004568 Johnson, Laverne C.; Spinweber, Cheryl L. Naval Health Research Center, San Diego, CA **Effects of a short-acting benzodiazepine on brain electrical activity during sleep.** Springfield, VA, NTIS, AD-A101 786/2, 1980. 17 p.

The effects of the short-acting benzodiazepine, triazolam, on EEG activity during sleep was assessed in poor sleepers. Twenty male Ss, mean age 21 plus or minus 2.37 years, participated in a screening night which preceded three placebo nights, six treatment nights, and two placebo withdrawal nights. During a double-blind treatment condition, 10 Ss received triazolam (0.5mg) and 10 Ss received placebo. In addition to rate/

min spindle count and number of delta half-waves/min, the auditory evoked response (AEP) was obtained on the last placebo baseline and on drug night 5. Ss receiving triazolam showed a significant increase in sleep spindles and a significant decrease in delta count during drug administration. Both values returned to baseline on the first withdrawal night. The AEP peak to trough amplitude was also significantly reduced during sleep by triazolam, but, as the time since drug ingestion increased, the amplitude of the AEP also increased. There was no difference in AEP amplitude between the two groups 5 hours postdrug ingestion. (Journal abstract modified)

004569 Lavie, P.; Wajsbort, J.; Youdim, M. B. H. Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel **Deprenyl does not cause insomnia in parkinsonian patients.** Communications in Psychopharmacology. 4(4):303-307, 1980.

The effects of deprenyl treatment on electrophysiological sleep parameters in parkinsonian patients were investigated. Deprenyl (10mg daily) was given to 10 parkinsonian patients treated with L-dopa. Whole night EEG, electrooculographic, and EMG recordings of each patient were analyzed to evaluate sleep structure before treatment and 14 days after treatment had begun. Deprenyl significantly shortened sleep latency without affecting any of the other sleep parameters. Since deprenyl inhibits platelet monoamine oxidase (MAO) activity by almost 100% in all patients, it can be concluded that suppression of MAO type-B activity does not adversely affect sleep structure. 16 references. (Author abstract modified)

004570 Loftus, Elisabeth F. no address **/Memory: the effects of alcohol and of marihuana./** Memoire: les effets de l'alcool et de la marijuana. Psychologie. No. 124:26-32, 1980.

Studies on the effects of marihuana and alcohol on short-term and long-term memory are reviewed. Studies on memory focus on three factors: short-term memory; the ability to transfer information from short-term to long-term memory; and the ability to retrieve information from the long-term memory bank. Experiments by Ben Jones show that alcohol has no effect on short-term memory, but does affect the transfer of information into the long-term memory bank. An experiment by Birnbaum and Parker shows no significant effect of alcohol on long-term memory. Experiments concerning alcoholic blackout show that the transfer from short-term to long-term memory is severely affected. Studies on the effects of marihuana on memory have shown that it affects both short-term memory, and the transfer from short-term to long-term memory.

004571 Mamelak, Mortimer; Webster, Peter. Sunnybrook Medical Centre, University of Toronto Clinic, 2075 Bayview Ave., Toronto, Ontario, Canada **Treatment of narcolepsy and sleep apnea with gammahydroxybutyrate: a clinical and polysomnographic case study.** Sleep. 4(1):105-111, 1981.

The use of gammahydroxybutyrate (GHB) for narcolepsy associated with central sleep apnea in a 53-year-old patient is discussed. The treatment relieved the major symptoms of narcolepsy and significantly decreased the number of apneic periods. GHB did not cause the prolonged and potentially fatal apneic periods associated with the use of other hypnotic agents. If GHB acts by promoting the integration of sleep then its stabilizing effect on respiration becomes understandable. Findings indicate that GHB can be used to advantage in the management of patients with narcolepsy/cataplexy and central type sleep apneas. 14 references. (Author abstract modified)

004572 Man'kovskiy, N. B.; Weinstock, A. B.; Malinovskaya, N. B. Otdeleniye vozrastnoy fiziologii i patologii nervnoy sistemy, Institut gerontologii AMN SSSR, Kiev, USSR **/Prospects for the treatment of postencephalitic parkinsonism with antilymphocytic immunoglobulin./** Perspektivy lecheniya postentsefaliticheskogo parkinsonizma antilimfotsitarnym immunoglobulinom. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(2):175-180, 1980.

The treatment of postencephalitic parkinsonism with antilymphocytic immunoglobulin (ALG) was studied in 25 patients (35 to 60 years old) and in a control group. Before treatment with ALG the Ss showed signs of the progression of extrapyramidal pathology. Previous treatment had been inadequate. Results show that the autoimmune mechanism plays an important role in the pathogenesis of postencephalitic parkinsonism. The use of ALG has a positive effect on the basic symptoms of the disease (impaired movement, trembling, and autonomic disturbances). Results also show that in some cases the use of ALG makes it possible to cease or significantly reduce doses of antiparkinsonism medications. 12 references.

004573 Maoz, B.; Durst, N. Psychiatry Dept., Soroka Medical Center, Beer Sheba, Israel **The effects of oestrogen therapy on the sex life of post-menopausal women.** Maturitas. 2:327-336, 1980.

The literature concerning sexual behavior around the time of menopause is reviewed, with emphasis on the effects of estrogen therapy on the sex lives of post menopausal women. A decline in sexual activity and satisfaction in women which is attributed to physiological changes is described. Data were obtained from 40 women who were treated with estrogens for 1 year. The effect of this treatment on sexual activity and satisfaction was compared to that of a group who had undergone partial estrogen treatment only. The results show that the former group experienced a reduction in symptoms such as hot flushes and depression, and the pain in sexual intercourse was removed. As a consequence of this improvement, coital activity and satisfaction were more gratifying in this group. The partially treated Ss in the second group showed a clear decline in sexual activity and satisfaction. 11 references. (Author abstract modified)

004574 Nicholson, A. N.; Stone, Barbara M. Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire, England **A synthetic ACTH4-9 analogue (Organon 2766) and sleep in healthy man.** Neuropharmacology. 19(12):1245-1246, 1980.

The effects of a synthetic ACTH4-9 analogue (Organon 2766) on sleep parameters were investigated in young adult males. Each of six Ss ingested 40mg, 80mg, and 120mg Organon 2766, 300mg caffeine, and matching placebos with water 20 minutes before retiring. Seven days separated each assessment, and the study was double-blind with treatments presented in random order. Organon 2766 in doses up to 120mg had no effect on the sleep process as indicated by conventional EEG techniques, although within this dose range (40mg) it has been reported to improve vigilance of Ss in a reaction time task. 9 references

004575 no author. Office on Smoking and Health, Public Health Service, U.S. Dept. of Health and Human Services, Rockville, MD 20857 **/The role of nicotine in the behavioral aspects of cigarette smoking./** Behavioral aspects. In: Surgeon Gen., The changing cigarette: health conseq. of smoking. Washington, GPO, DHHS Publication No. (PHS)81-50156, 1981. (p. 175-192).

It is recommended that research on lower tar and nicotine cigarettes should take the following steps in the future: 1) additional laboratory studies should be performed under controlled experimental conditions; 2) additional research should be conducted on compensatory smoking; and 3) both the biological and psychological factors involved in smoking should be investigated. Facilities and research cigarettes, which are needed to determine the behavioral aspects of smoking, are described. Research is reviewed which shows that: 1) nicotine appears to be the primary pharmacological reinforcer in tobacco, but other pharmacological and psychosocial factors also may contribute a reinforcing effect; 2) it appears that some smokers make compensatory adjustments in their smoking behavior with cigarettes of different yields that might increase the amounts of harmful substances entering the body; 3) additional information is needed on the role of lower tar and nicotine cigarettes in the initiation, maintenance, and cessation of smoking; and 4) the development of improved laboratory facilities is necessary for more tightly controlled behavioral research and smoking machine measurements that more closely simulate the practices of human smokers. 82 references.

004576 Nyhan, William L.; Johnson, Harold G.; Kaufman, Irving A.; Jones, Kenneth Lyons. Dept. of Pediatrics, University of California at San Diego, La Jolla, CA 92093 **Serotonergic approaches to the modification of behavior in the Lesch-Nyhan syndrome.** Applied Research in Mental Retardation. 1(1/2):25-40, 1980.

In a series of nine male patients with the Lesch-Nyhan syndrome, a pharmacologic attempt was made to alter the balance of biogenic amines in the central nervous system by increasing the level of serotonin. Patients were treated with 5-hydroxytryptophan in combination with a peripheral decarboxylase inhibitor carbidopa and with imipramine. Most patients had a striking alteration in self-mutilative behavior. However, within 1 to 3 months, each became tolerant and this pharmacologic effect could not be produced again even a year later. These observations suggest that the characteristic behavior of the patient with the Lesch-Nyhan syndrome is related to neurotransmitter balance, and that there may be ways to modify it. 19 references. (Author abstract)

004577 Rosen, Alexander J.; Mueser, Kim T.; Sussman, Steve; Davis, John M. Psychology Department, University of Illinois at Chicago Circle, Chicago, IL 60680 **The effects of neuroleptic drugs on the social interactions of hospitalized psychotic patients.** Journal of Nervous and Mental Disease. 169(4):240-243, 1981.

The frequency of social interactions emitted by two groups of hospitalized psychotic patients was studied with a time sampling procedure during lunch periods in the ward dayroom. One group was treated with neuroleptic medication upon admission to the ward, and the other group was medicated after a 2-week to 3-week washout period. The data suggest that the principle effect of the medication is to produce a transient depression in social interaction frequency which returns to baseline with continued drug treatment. The results are supportive of previous research which indicated that the major impact of pharmacotherapy is on activity rather than social behaviors, and highlights the utility of including baseline measures to ensure adequate drug vs. control comparisons. 16 references. (Author abstract)

004578 Rosenzweig, M. R.; Bennett, E. L.; Flood, J. F. Lawrence Berkeley Laboratory, University of California, Berkeley, CA 94720 **Pharmacological modulation of formation of long-term memory.** Springfield, VA, NTIS, LBL-11558, 1980. 12 p.

Biochemical processes that can modulate the formation of long-term memory, including the synthesis of proteins, are considered. Schemes of memory formation involving several stages have been proposed and specific mechanisms have been hypothesized to account for these stages. Evidence supporting the existence of such stages has been found. The hypothesis that protein synthesis is required for formation of memory has stimulated much research and several recent reviews. But many treatments and agents that have been found to affect the formation of memory cannot be incorporated directly into this sequence of presumed basic processes. While this and other reasons have led some investigators to question or even abandon the hypothesized basic sequence, other investigators have taken up the concept that modulatory as well as basic processes exist. That is, the processes required for formation and expression of memory take place within a complex bodily environment where other systems or processes can influence or modulate those that participate directly in the formation of memory. (Author abstract modified)

004579 Shutov, A. A.; Pleshkova, N. M.; Prostakova, T. I. Permskiy meditsinskiy institut na baze oblastnoy klinicheskoy bol'nitsy, Perm, USSR **/Correction of hormonal activity of the thyroid gland as a method of pathogenic therapy in a comprehensive treatment of patients with temporal epilepsy./** Korrektsiya gormonal'noy aktivnosti shchitovidnoy zhelezy kak metod patogeneticheskoy terapii v komplekse lecheniya bol'nykh visochnoy epilepsiyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(8):1016-1020. 1979.

Corrective therapy with thyroidin and diiodothyrosine of disturbed hormonal activity of the thyroid gland was carried out in 30 patients with temporal epilepsy. There was a favorable therapeutic effect within 1.5 years: the epileptic paroxysms either disappeared or their frequency was reduced; significant normalization of the EEG and iodine metabolism occurred; and improvement in the patients' mental state was observed. It is recommended that the comprehensive treatment of patients with temporal epilepsy include hormonal correction of thyroid gland activity. 3 references. (Journal abstract modified)

004580 Silverstone, T.; Fincham, Jill; Wells, B.; Kyriakides, Mary. Academic Unit of Human Psychopharmacology, Medical Colleges of St. Bartholomew's, London, England **The effect of the dopamine receptor blocking drug pimozide on the stimulant and anorectic actions of dextroamphetamine in man.** Neuropharmacology. 19(12):1235-1237, 1980.

The effects of the dopamine receptor blocking drug pimozide on the stimulant and anorectic actions of dextroamphetamine were investigated in eight healthy female Ss. A single 10mg oral dose of d-amphetamine caused a significant increase in ratings of arousal, and a decline in hunger. The effect of d-amphetamine on arousal was diminished by 2mg oral dose of pimozide administered 2 hours before the d-amphetamine was taken. It is concluded that dopamine mechanisms in the CNS are involved in the mediation of the stimulant effects of d-amphetamine in man, but not in the mediation of d-amphetamine-induced anorexia. 10 references.

004581 Singh, Vimal Kumari; Gupta, B. S. Dept. of Psychology, Institute of Advanced Studies, Meerut University, Meerut, India **Personality and drugs in visual figural aftereffects.** International Journal of Psychology. 16(1):35-44, 1981.

The effects of dexedrine and phenobarbitone on visual figural aftereffect (VFAE) were examined in 32 postgraduate Ss tested on the Maudsley Personality Inventory. Calcium tablets were used as placebos. Ss were tested repeatedly under each of the treatment conditions. The results indicated that: 1) extraverted Ss relative to introverted Ss have larger VFAEs; 2) the size of VFAE increases under the influence of phenobarbitone in all personality groups except high positive neuroticism/high extroversion and low neuroticism/low extroversion; and 3) interactions between drug treatments and personality variables in their effects on VFAE did not occur. 30 references. (Author abstract modified)

004582 Stitzer, Maxine L.; Griffiths, Roland R.; Bigelow, George E.; Liebson, Ira. Dept. of Psychiatry, D-5-West, Baltimore City Hospitals, Baltimore, MD 21224 **Human social conversation: effects of ethanol, secobarbital and chlorpromazine.** Pharmacology Biochemistry and Behavior. 14(3):353-360, 1981.

Effects of oral ethanol, secobarbital, and chlorpromazine on human vocalization were studied in dyadic social situations, using repeated observations within subject pairs. Ethanol (1 to 6 oz of 95 proof) and secobarbital (30 to 300mg) produced dose related increases in vocalization by the S who received the active drug and had no systematic effects on the partner who received the placebo. Chlorpromazine (25 to 100mg) produced dose related decreases in vocalization by the S given the active drug and tended to decrease vocalization by the partner receiving the placebo. No consistent changes on the Addiction Research Center Inventory scales were obtained after ethanol or secobarbital, but chlorpromazine produced dose related increases on the Pentobarbital, Chlorpromazine, and Alcohol Group scale. It is concluded that quantitative measures of vocalization (converational speech) in a social context is a reliable and sensitive indicator of dose related drug effects. 27 references. (Author abstract modified)

004583 Timsit-Berthier, M.; Mantanus, H.; Jacques, M. C.; Legros, J. J. Laboratoire de Neurophysiologie, Clinique et de Psychopathologie, Boulevard de la Constitution 153, B-4020 Liege, Belgium **/Use of lysine-vasopressin in the treatment of posttraumatic amnesia./** Utilite de la lysine-vasopressine dans le traitement de l'amnesie post-traumatique. Acta Psychiatrica Belgica. 80(5):728-747, 1980.

Seven subjects suffering from posttraumatic amnesia were treated with lysine-vasopressin as a nasal spray for 15 days (14 UI per day). All subjects (males, aged 20 to 63) previously presented a deficit for 3 years, did not follow any treatment, and did not hope for any improvement. Five subjects presented a real improvement, either immediately during the treatment, or some weeks after the treatment. Improvement was evidenced by psychological tests of attention and short-term visual retention and by electrophysiological measurements. Improvement was mainly on general activity, motivation, and capacity for social adaptation and was associated in four subjects with a marked increase in the level of neurophysine I. The mode of action of lysine-vasopressin is discussed in light of recent neurochemical and neurophysiological research. 19 references. (Author abstract modified)

004584 Tsygankov, B. D. Otdel terapii psikhozov, Moskovskiy NII psikhiatrii, Ministerstvo zdravookhraneniya RSFSR, Moskva, USSR **/A modified version of the simultaneous discontinuation of psychotropic drugs (combined with the administration of diuretics) as a method of halting prolonged attacks of schizophrenia./** Modifitsirovannyy variant odnomomentnoy otmeny psikhotropnykh sredstv (v sochetanii s priyemom diuretikov) kak metod obryvayushchey terapii zatyazhnykh pristupov shizofrenii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(5):754-759, 1980.

The sudden discontinuance of psychotropic drugs (combined with the administration of diuretics) as a method of halting prolonged attacks of schizophrenia was studied in 100 schizophrenic patients who were resistant to psychopharmacotherapy. The efficacy of intense psychopharmacotherapy was compared to the efficacy of the discontinuance therapy. Results show that the discontinuance therapy appeared to be the most effective and to have the fewest side-effects. 13 references. (Journal abstract modified)

004585 Waid, William M.; Orne, Emily Carota; Cook, Mary R.; Orne, Martin T. Institute of Pennsylvania Hospital, 111 North 49 Street, Philadelphia, PA 19139 **Meprobamate reduces accuracy of physiological detection of deception.** Science. 212(4490):71-73, 1981.

The effects of a tranquilizer, meprobamate, on polygraph test results were studied. Normal male Ss attempted to deceive an experimenter recording electrodermal, respiratory, and cardiovascular activity. Those who had ingested a placebo or nothing were detected with statistically significant frequency on the basis of their phasic electrodermal responses, which clearly distinguished them from truthful suspects. That was not the case with deceptive Ss who had ingested 400 milligrams of meprobamate, nor did the examiner detect which Ss had received the drug. 24 references. (Author abstract modified)

004586 Weisner, B.; Bernhardt, W. Bernhardt: Neurologische Universitatsklinik, Martinistrasse 52, D-2000 Hamburg 20, West Germany **Antiepileptic therapy with phenytoin: which is the optimum serum level?** European Neurology. 18(2):111-115, 1979.

The relationship between serum phenytoin level and anticonvulsant effects was studied in 114 patients suffering from generalized grand mal-seizures and treated only with phenytoin. The probability of attacks followed an exponential function of serum phenytoin. However, the high variability in responsiveness during serum phenytoin below 10mg/l suggested that the effective dose level must be determined separately and repeatedly for each patient. 19 references. (Author abstract modified)

004587 Wikler, Abraham. no address **Opioid dependence: mechanisms and treatment.** New York, Plenum, 1980. 225 p. L27.50.

Mechanisms and treatment of opioid dependency are examined in an extended review of the literature. Emphasis is placed on the neuropharmacological and behavioral aspects of dependence. It is proposed that relapse into drug dependence is a disease; factors contributing to relapse are considered. A long-lasting subtle abstinence syndrome, characterized by persistent conditioned autonomic responses is postulated. Elimination of this syndrome through extinction procedures is discussed.

15 TOXICOLOGY AND SIDE EFFECTS

004588 Ansell, G. B. Dept. of Pharmacology, University of Birmingham, Medical School, Birmingham B15 2TJ, England **The biochemical background to tardive dyskinesia.** Neuropharmacology. 20(4):311-317, 1981.

The treatment of tardive dyskinesia induced by long-term neuroleptic therapy is discussed. Since tardive dyskinesia is believed to be due to an imbalance in dopaminergic and cholinergic influences on the striatum, treatment of the disorder generally has involved blockade of excess striatal dopaminergic activity or enhancement of cholinergic activity in the same area. Recent clinical studies of neurological disorders such as Huntington's chorea and Alzheimer's disease have stimulated interest in the use of 2-dimethylaminoethanol, choline, and lecithin in the treatment of tardive dyskinesia. 65 references.

004589 Ansseau, M.; Diricq, St.; Grisar, Th.; Collard, J. Clinique Medico-Psychologique, Unite de Psychopharmacologie, Hopital universitaire de Baviere, B-4020 Liege, Belgium **Biochemical and neuroendocrine approaches to a malignant syndrome of neuroleptics.** Acta Psychiatrica Belgica. 80(5):600-606, 1980.

The case history is presented of a 20-year-old patient, hospitalized for depressive schizophrenia, who developed the malignant syndrome when treated with nomifensine plus pimozide. Clinical observations associated with the syndrome are noted and treatment is discussed. Results of the endocrine balance over the 2 week course of the illness suggest a hypothalamic perturbation involving an increase in the norepinephrine and dopamine proportions with a relative norepinephrine predominance. It is suggested that the malignant syndrome, which is normally attributed to a neuroleptic, may find its etiopathogeny in the association of a neuroleptic with an antidepressant. (Author abstract modified)

004590 Ayd, Frank J., Jr. 912 West Lake Avenue, Baltimore, MD 21210 **Neuroleptics and their side-effects.** Journal of Psychiatric Treatment and Evaluation. 1(2):25-27, 1979.

A review of the phenothiazine neuroleptics and their side-effects is presented. In order of milligram potency are the piperidines (thioridazine), the aliphatics (chlorpromazine), and the piperazines (fluphenazine). Low milligram potency neuroleptics such as fluphenazine are less likely to cause adverse effects and are more likely to be acceptable to the patient. Phenothiazines may cause a variety of sedative, autonomic, endocrine, dermatologic, ocular, hepatic, hematopoietic, and cardiovascular effects, as well as seizures and extrapyramidal reactions. The propensity to evoke these reactions depends on the chemical structure of the phenothiazine. Neuroleptic-induced extrapyramidal side-effects can be divided into early onset reactions such as akinesia, acute dyskinesia, akathisia, and parkinsonism, and late onset reactions of tardive dyskinesia.

004591 Bailey, David N. University of California, San Diego, La Jolla, CA 92093 **Chlorpromazine analysis in human plasma. (Unpublished paper).** Final Report, NIMH Grant 5R01-MH-30943, 1980. 15 p.

Methods were developed for analysis of chlorpromazine, phencyclidine, tricyclic antidepressants, meprobamate, and theophylline levels in human sera. The methods are applicable to therapeutic dosages and overdose concentrations. Gas and liquid chromatography with a nitrogen phosphorus detector and ultraviolet spectrophotometric procedures were used. Data are presented on the assay development, assay specifications, and application of the assay to patients receiving drug therapy and to Ss receiving emergency toxicology services. A profile of the average drug abuse patient was developed, and information was obtained on drugs ingested and the serum drug concentrations. Findings from separate hospitalizations were compared and characteristics of the typical repeating drug abuser were identified. 14 references.

004592 Berger, Philip A. Dept. of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305 **Tardive dyskinesia: recent developments.** International Drug Therapy Newsletter. 15(5):17-20, 1980.

Recent developments in the diagnosis, neuropathology, and treatment of tardive dyskinesia (TD), the most troublesome complication limiting the use of maintenance neuroleptic therapy for psychiatric disorders, are reviewed. No unequivocal treatment for TD has been demonstrated, although ChCl, lecithin, deanol, low dose apomorphine, and high dose levodopa desensitization show promise. The suggestion that lithium salts may prevent the development of TD requires testing. The assumption that continuation of neuroleptic treatment invariably worsens TD has not been rigorously demonstrated. It is suggested that the clinician should probably discontinue neuroleptics in some cases of TD. The acute with schizophreniform psychosis is seen as possibly not needing the drugs after symptom resolution. Chronic hospitalized patients who are nonresponders or who are only minimally responsive might also be better off without neuroleptics. It is suggested that the clinician should continue neuroleptics but should discontinue anticholinergics in some patients for whom the return of psychosis is more detrimental than are TD symptoms, and that this judgment should be made by both physician and patient (who should confirm in writing his understanding of the relative risks). 138 references.

004593 Boldyrev, A. I.; Fleys, E. P.; Vayntrub, M. Ya. Klinika epilepsii, Moskovskiy NII psikhiatrii, Ministerstvo zdravookhraneniya RSFSR, Moskva, USSR /**Neurological complications due to the pharmacological treatment of epileptic patients.**/ Nevrologicheskiye oslozhneniya pri medikamentoznom lechenii bol'nykh epilepsiyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(6):738-741, 1979.

Neurological complications due to anticonvulsant treatment were analyzed in 48 epileptic patients. There were functional disturbances of the brainstem and cerebellar neuronal systems; disarticulation (apparently caused by pseudobulbar syndrome); and muscle relaxation (particularly in patients receiving benzodiazepines) connected with disturbances of the spinal reflex mechanisms. In 22 of the Ss there were symptoms of damage both to the CNS and the peripheral nerves. Results show that the onset of neurological complications is accompanied by a changed structure and increased frequency of epileptic seizures, and that residual signs of organic diseases are important diagnostically. 8 references. (Journal abstract modified)

004594 Braccini, T.; Coat, C.; Lavagna, J.; Myguel, M.; Dascourt, G. Service de Psychiatrie et de Psychologie Medicale, Hopital Dasteur, F-06031 Nice Cedex, France /**Neurological tolerance of lithium and psychotropic drugs in combination: 265 cases.**/ Tolerance neurologique de l'association lithium-psychotropes: a partir de 265 cures associatives. Encephale. 7(1):29-43, 1981.

Neurological tolerance for combined lithium/psychotropic drug treatment was studied retrospectively in 265 cases in 132 patients between 1971 and 1978. In comparison with other combinations, neurological tolerance is not increased when haloperidol is combined with lithium. However, the presence of cerebral lesions is a risk factor. One hundred seventeen cases of combined treatment were preceded by treatment with either lithium or a psychotropic drug. An analysis of these cases showed that cases of intolerance doubled when combination therapy was begun, and that the neurological effects increased in intensity. 15 references. (Journal abstract modified)

004595 Branchey, Marc H.; Branchey, Laure B.; Richardson, Mary Ann. Alcoholism Research and Treatment Center, V.A. Hospital, 130 West Kingsbridge Rd., Bronx, NY 10468 **Effects of neuroleptic adjustment on clinical condition and tardive dyskinesia in schizophrenic patients.** American Journal of Psychiatry. 138(5):608-612, 1981.

Attempts to decrease neuroleptic medication were made in 21 chronic schizophrenic patients in order to minimize the risks of tardive dyskinesia. Level of psychopathology and severity of dyskinetic symptoms were monitored while the neuroleptic was gradually decreased over 3 months and then discontinued. Only one patient relapsed during drug decrease, but 15 patients relapsed within 6 months after drug withdrawal. After relapse, medication was gradually increased. The doses needed to induce recovery were higher than those which had been sufficient to prevent relapse during gradual drug reduction. Dyskinetic symptoms were not significantly modified during drug reduction but increased significantly after drug discontinuation. 13 references. (Author abstract modified)

004596 Bron, Bernhard. Psychiatrische Universitatsklinik, v.-Siebold-Strasse 5, D-3400 Gottingen, West Germany /**Drug-induced psychosis and schizophrenia in adolescents.**/ Drogeninduzierte Psychose und Schizophrenie im Jugendalter. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie. 126(1):179-197, 1980.

Among 233 young drug abusers with different drug-induced psychotic syndromes, there were 84 patients whose psychosis showed a character of its own. Their drug history and behavior, life history (including in some cases premorbib personality signs), psychotic diseases in their families, and psychopathological diagnosis showed statistically significant differences relative to other patients. The stage of development can be an especially relevant prepsychotic circumstance if it is influenced by drugs. There are a number of unanswered questions, for example, why do some patients with similar or equal prerequisites become drug abusers, while others have a psychosis having its own laws. The cause of drug-induced psychosis with its own laws among young people needs to be considered in several dimensions: effects of the drug, individual constitutional factors, specific personality factors, psychodynamic and reactive aspects in situations, and specific and typical developmental factors. Clinical observations show essential connections between drug effects and a psychosis having its own laws. 44 references. (Journal abstract modified)

004597 Burgess, C. D.; Turner, P. Dept. of Clinical Pharmacology, University of Southampton, Centre Block, Southampton General Hospital, Southampton S09 3TU, England **Cardiotoxicity of antidepressant drugs.** Neuropharmacology. 19(12):1195-1199, 1980.

The effects of different groups of antidepressant drugs on the cardiovascular system (CVS) are reviewed, and clinical implications of these CVS effects are discussed. In addition to the CVS effects of the tricyclic antidepressants, the effects of maprotiline, mianserin, monoamine oxidase inhibitors, lithium, nomifensine, and zimelidine are discussed. It is noted that serious cardiovascular complications do not occur frequently after therapeutic doses, but that after overdose, many of these agents may prove lethal. The more serious complications are more likely to occur in the aged and in those with cardiovascular disease. 63 references. (Author abstract modified)

004598 Carranza, J. University of Mississippi, Medical Center, 2500 North State Street, Jackson, MS 39216 **Long term use and abuse of benzodiazepines.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(5):254-258, 1980.

The long-term use and abuse of benzodiazepines are discussed. The detrimental effect that lay publications, television, and the mass media has had on the pharmacotherapy of anxiety and depressive reactions with benzodiazepines is emphasized. A case study is provided of a patient who was suffering from anxiety attacks, agoraphobia, and fear of dying and was treated successfully with Librium for a long period, but who eventually refused Librium for fear of his possible addiction to the drug. In a review of the literature, few well documented cases of benzodiazepine dependence have been found. It is suggested that the seizures that are reported with withdrawal of benzodiazepines after long-term use is clinical evidence of the anticonvulsant effect of benzodiazepines and that this is not proof of a physical dependence. The withdrawal syndromes associated with high dosages of benzodiazepines might have a different neurochemical mechanism than that observed in alcohol and barbiturate withdrawal. 16 references.

004599 Chodera, A.; Cenajek, D.; Mazurek, K. Medical Academy Poznan, Dept. of Pharmacology, ul. Fredry 10, 61-701 Poznan, Poland **Interaction of p-chlorophenylalanine, mianserine and danitracen with amphetamine.** Arzneimittel-Forschung. 31(1):61-63, 1981.

Three antiserotonin compounds, p-chlorphenylalanine, mianserin, and danitracen, were investigated for their influence on amphetamine stereotype in correlation with concentration of this amine in blood serum and brain tissue. A positive correlation (decrease in stereotypy and in the concentration of amphetamine in serum and brain) was found only for danitracen. P-chlorphenylalanine and mianserin premedication decreased serum and brain tissue concentrations of amphetamine, but enhanced the amphetamine stereotypy effect. It is assumed that in the mixed pharmacodynamic/pharmacokinetic interaction in the case of mianserin and p-chlorphenylalanine the pharmacodynamic component (inhibition of the serotoninergic system in CNS) prevails, whereas in the case of danitracen the pharmacokinetic effect is superior. 10 references. (Journal abstract)

004600 Cohen, Martin; Dailey, George; Meshad, Michael; Renick, John; Kreisberg, Robert. Dept. of Psychiatry, University of Iowa, College of Medicine, Iowa City, IA 52242 **In normal young men acute dopaminergic blockade does not impair free water excretion following a standard water load.** Communications in Psychopharmacology. 4(4):323-326, 1980.

The hypothesis that water intoxication in psychiatric patients is a side-effect of the dopaminergic blockade of psychotropic medication was evaluated in nine healthy volunteer Ss. The administration of 1mg haloperidol intramuscularly produced markedly increased serum prolactin levels but had no effect on the ability of normal volunteers to excrete a water load. This is consistent with difficulties in demonstrating in man any effects on water and electrolyte metabolism of increasing endogenous levels of prolactin with thyroid releasing hormone stimulation. These results do not preclude the possibility that the effects of dopaminergic blockade might become manifest only over an extended time period. 11 references. (Author abstract modified)

004601 Cole, Jonathan O. Psychopharmacology Program, McLean Hospital, Belmont, MA 02178 **Prevention of tardive dyskinesia and other drug-related adverse effects.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 353-363).

The prevention of the side-effects of tardive dyskinesia (TD), agranulocytosis, and sudden death during antipsychotic (AP) drug treatment for schizophrenia is discussed. Important issues discussed include: 1) the exact relationship between drug exposure and the presence of TD; 2) drug holidays; 3) evaluation of low dose AP drug therapy; and 4) establishment of lowest effective maintenance dosage. Treatment of TD and some alternate drug therapies are considered. It is suggested that some of these problems warrent multihospital collaborative studies based on a single protocol while others are more appropriate for research units in single hospitals. A discussion of the paper follows. 30 references. (Author abstract modified)

004602 Dam, Mogens. University Dept. of Neurology, Hvidovre Hospital, Hvidovre, Denmark **/Various aspects of the effect of anticonvulsant drugs on memory./** Additional aspects. Acta Neurologica Scandinavica. 62(Suppl. 80):56-57, 1980.

Comments are made on several aspects of the effect of antiepileptic drugs on memory function. It is argued that many of the reactions may be caused by the disease itself or by a combination of the drug and epilepsy, and that there is a need for further investigations to ascertain definite drug-induced side-effects in such coumpounds, as phenytoin. Evidence is briefly reviewed on the psychotropic effects of carbamazepine, and it is concluded that the compound is neuropsychologically most useful in patients with below average intelligence who show signs of emotional disturbance.

004603 Davis, John M.; Janicak, Philip G.; Killian, Grant A. Illinois State Psychiatric Institute, Chicago, IL 60612 **Clinical strategies for antipsychotic drug treatment, tardive dyskinesia, and the training of research psychiatrists.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 365-383).

The issue of neuroleptic treatment and tardive dyskinesia is examined from the viewpoint of developing clinical research strategies to improve treatment and minimize side-effects. The problem of training psychiatrists in clinical research is discussed. Several suggestions including rare patient protocols, registries, and record keeping are discussed in the context of projects which are deemed feasible in both the state and federal systems of psychiatric care. Such a model could alleviate the critical shortage of psychiatrists trained in good clinical research. A discussion of the paper follows. 35 references. (Author abstract modified)

004604 Davis, Kenneth L.; Berger, Philip A.; Hollister, Leo E. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA **Clinical and preclinical experience with choline chloride in Huntington's disease and tardive dyskinesia: unanswered questions.** In: Barbeau, A., Nutrition and brain. New York, Raven Press, 1979. v. 5. (p. 305-315).

A review is presented of preclinical and clinical research into the potential of choline chloride treatment of tardive dyskinesia and Huntington's disease. Investigations establishing the transitory efficacy of the acetylcholinesterase inhibitor, physostigmine, in several neuropsychiatric disorders, have stimulated further research aimed at discovering a safe, long acting oral cholinomimetic. Evidence in this area of study is reviewed, including that relating to: the effect of choline on central cholinergic activity; the efficacy of choline in treatment of tardive dyskinesia; the relationship between choline administration and plasma and cerebrospinal fluid choline levels; the mechanisms underlying the symptomatic improvement of tardive dyskinesia associated with increased cholinergic activity. Implications of these data are discussed with reference to the hypothesis that cholinomimetics inhibit nigrostriatal dopamine impulse flow. Possible long-term effects of choline treatment are discussed, and the need for further research is noted. (Author abstract modified)

004605 Deiser, Roland; Schindler, Raoul. Schindler: Psychiatrisches Krankenhaus der Stadt Wien, Baumgartner Hohe 1, A-1145 Wien, Austria /**The course of long-term treatment with fluphenazine decanoate (Dapotum-D).**/ Das Verlaufsbild langjähriger Behandlungen mit Fluphenazindekanoat (Dapotum D). Psychiatria Clinica. 13(3-4):193-205, 1980.

Data are provided on the course of long-term treatment of 76 psychiatric patients using fluphenazine decanoate. Objective and subjective tolerance following 5 years or more of treatment were compared in patients exhibiting continuous ambulatory adjustment, in those with continuous inpatient adjustment, and in those who withdrew from the drug or changed the medication after 5 years or more of permanent adjustment. A significant stabilization in the clinical picture and a good permanent compatibility (reduction in objective side-effects) were demonstrated. Complete withdrawal of permanent medication caused late dyskinesias and a tendency to slow remission in 36.9% of the patients. The latency of this development is seen as binding both physician and patient to the successful completion of therapy. 19 references. (Journal abstract modified)

004606 Deutsch, Stephen I.; Peselow, Eric D.; Banay-Schwartz, Miriam; Gershon, Samuel; Virgilio, Joanne; Fieve, Ronald R.; Rotrosen, John. Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Effect of lithium on glycine levels in patients with affective disorders.** American Journal of Psychiatry. 138(5):683-684, 1981.

Evidence is reported in support of an abnormality in glycine regulation in RBCs from patients with bipolar depression. The findings suggest that this effect results from lithium treatment in affective disordered patients, and that the abnormality occurs only in bipolar patients and not in those with recurrent unipolar major depressive disorders. The possible mechanisms responsible for the observed increases in erythrocyte glycine are suggested, and it is concluded that further biochemical research should be conducted in light of glycine's role as a neurotransmitter. 10 references.

004607 Elsass, Peter; Mellerup, Erling T.; Rafaelsen, Ole J.; Theilgaard, Alice. Clinical Psychological Unit, Dept. of Psychiatry, Rigshospitalet, 9, Blegdamsveij, DK-2100 Copenhagen O, Denmark **Effect of lithium on reaction time – a study of diurnal variations.** Psychopharmacology. 72(3):279-282, 1981.

Continuous reaction time performance was measured in groups of manic-depressive patients treated with lithium, control manic-depressive patients treated with other drugs or no drugs, and normal controls. Reaction times in patients treated with lithium were slower than those of the normal and psychiatric controls. However, the effect of lithium on reaction times was weaker than that of diazepam sedation, organic brain damage, or hepatic encephalopathy. For all three groups, reaction times were slower in the morning than in the evening or at night. Slow reaction times at initial testing were correlated with relatively large variations over 24 hours for normal and psychiatric controls, but not for the patients treated with lithium. 18 references. (Author abstract modified)

004608 Endo, Masaomi; Hirano, Masaharu; Nakamura, Ichiro; Kawai, Yoshiharu. Dept. of Neuropsychiatry, Toyama Medical and Pharmaceutical University, Faculty of Medicine, Toyama, Japan **The two survival cases of alpha-pattern coma caused by large amounts of hypnotics and neuroleptics.** Folia Psychiatrica et Neurologica Japonica. 34(4):451-458, 1980.

The EEGs of two men aged 42 and 63 who survived overdoses of hypnotic and neuroleptic drugs are described. The EEGs of the two Ss initially demonstrated alpha pattern coma. The prominent pattern of the EEG changes from the alpha to a theta pattern and subsequently into a low amplitude alpha pattern. The patients recovered from the suicide attempt without any residual neurological symptoms. These findings suggest that the outcome of alpha pattern coma induced by drug poisoning is favorable, and it is concluded that a longitudinal EEG recording should be performed as early as possible when the patient is in a comatose state. 22 references. (Author abstract modified)

004609 Fariello, Ruggero G. Clinical Neurophysiology, Dept. of Neurology, University of Wisconsin, 600 Highland Ave., Madison, WI 53792 **Epileptogenic properties of enflurane and their clinical interpretation.** Electroencephalography and Clinical Neurophysiology. 48(5):595-598, 1980.

Three cases of EEG changes induced by a single exposure to enflurane anesthesia are reported. In one patient, enflurane administered during a donor nephrectomy resulted in unexpected partial motor seizures; until the cause of the seizures was correctly identified, the patient was inappropriately treated with anticonvulsants. Two other patients suffered from partial, complex, and generalized seizures uncontrolled by medication. Epileptic foci delineated and activated by enflurane were surgically ablated, and the patients are now seizure free. These findings indicate that enflurane exposure may cause mistakes in clinical interpretation of the EEG and that enflurane may be a useful tool in identifying epileptic foci during corticography or depth electrode intraoperative recordings. 7 references.

004610 Fraser, H. F,; Gorodetzky, C. W.; Kay, D. C.; Yeh, S. Y.; Dewey, W. L. Division of Research, Addiction Research Center, National Institute of Drug Abuse, Lexington, KY **Possible influence of opioid normetabolites on the onset, magnitude and quality of the opioide abstinence syndrome.** Drug and Alcohol Dependence. 5:255-272, 1980.

Drug dependence is viewed as a dynamic state which may be altered with time respecting pattern, magnitude, and quality of physical dependence due in part to the interaction of the parent opioid with its normetabolites. The principal metabolites of acetylmethadol were noracetylmethadol and dinoracetylmethadol and they were found to be active morphine-like agonists. Their long half-life and accumulation in the plasma accounted for the delayed onset of abstinence after the acetylmethadol was withdrawn. The normetabolites of propoxyphene, norpropoxyphene, and dinorpropoxyphene were found to be very weak morpine-like agonists. Normeperidine was inactive as a morphine-like agonist and appeared to have a different action in that it primarily is a convulsant. Although the formation and accumulation of normeperidine may account partly for the characteristics of its abstinence syndrome, a dominant factor was found to be the disappearance of meperidine from blood plasma. In the case of normorphine, norcodeine, and norlevorphanol, the difficulties in direct addiction tests in man are discussed. Examination of the source of abstinence scores for subcutaneous normorphine oral norcodeine, oral codeine, oral morphine, subcutaneous morphine, and oral methadone suggested that these compounds may be divided into two categories: normorphine and norcodeine in one category, and methadone in the other. The relevance of these observations to comparative studies of opioid abuse is discussed. (Journal abstract modified)

004611 Freeman, H. L.; Soni, S. D.; Carpenter, L. Dept. of Psychiatry, University of Manchester School of Medicine, Hope Hospital, Salford M6 8HD, England **A controlled trial of oxypertine in tardive dyskinesia.** International Pharmacopsychiatry. 15(5):281-291, 1980.

The effects of oxypertine in treating tardive dyskinesia were investigated. The design was double-blind, placebo controlled, between patient, in 28 patients from whom previous medication was withdrawn, with 14 patients in each group. Treatment was for 4 weeks. Although more oxypertine patients improved than placebo, 71.4% versus 50%, the results did not reach statistical significance. A further study is planned to increase the overall number of patients in the study, and to lengthen treatment periods. It is concluded that the results already add further weight to the previously existing evidence that oxypertine is of therapeutic value in the management of tardive dyskinesia. 15 references. (Author abstract modified)

004612 Gelenberg, Alan J.; Wojcik, Joanne Doller; Growdon, John H. Dept. of Psychiatry, Harvard Medical School, Boston, MA 02114 **Lecithin for the treatment of tardive dyskinesia.** In: Barbeau, A., Nutrition and the brain. New York, Raven Press, 1979. Vol. 5. (p. 285-303).

The administration of exogenous choline or lecithin to increase CNS cholinergic tone in the treatment of tardive dyskinesia (TD) is discussed. Eight case histories illustrate patient reactions to choline and to lecithin. Lecithin appears to produce the same CNS effects observed with choline, while causing fewer adverse reactions. If lecithin is, in fact, an effective nontoxic agent to suppress the movements of TD, it could provide an acceptable solution until a less neurotoxic antipsychotic agent is found. Confirmation of the results will show that a dietary constituent can affect the levels of an important CNS neurotransmitter to a clinically useful degree, thus opening possibilities for greater understanding of neurophysiology and other medical therapies. 64 references.

004613 Gourevitch, M. Hopital de Maison-Blanche, 3, avenue Jean-Jaures, F-93330 Neuilly-sur-Marne, France **/Neuroleptic treatment as experienced by a psychiatrist./** Un traitement neuroleptique vecu par un psychiatre. Evolution Psychiatrique. 46(1):97-104, 1981.

A psychiatrist who suffered from acute delirious psychosis recounts her treatment with neuroleptic drugs. The first treatment consisted of the combined administration of haloperidol and chlorpromazine, and biperiden on an outpatient basis. This treatment induced serious physical and mental aberrations, and the patient herself stopped the treatment after 24 hours. When she was hospitalized, cyamemazine and haloperidol were prescribed and administered. Extrapyramidal side-effects were serious, but they diminished somewhat after the cyamemazine was discontinued. After being discharged, the patient took haloperidol and methotrimeprazine for 3 months. Memory lapses were frequent and serious. Altogether, the effects were serious and very disconcerting and continued beyond the period of treatment.

004614 Gualtieri, C. T.; Hawk, Barbara. Dept. of Child Psychiatry, North Carolina Memorial Hospital, Chapel Hill, NC 27514 **Tardive dyskinesia and other drug-induced movement disorders among handicapped children and youth.** Applied Research in Mental Retardation. 1(1/2):55-69, 1980.

The literature concerned with tardive dyskinesias and other movement disorders caused by chronic use of neuroleptics is reviewed, with emphasis on their occurrence in mentally retarded youth and children. What appears is a confusing array of anecdotal reports and uncontrolled studies, a heterogeneous array of children with a variety of diagnoses and movements, and a wide range of intercurrent problems and medications. Even if there were no such symptoms as tardive dyskinesia, extrapyramidal symptoms, or withdrawal emergent symptoms, caution would still be advisable in the application of neuroleptic drugs among young people. Effects on the child's general demeanor, level of alertness, personality, and learning patterns would mitigate against the use of these agents except in carefully chosen circumstances. 57 references. (Author abstract modified)

004615 Hiroz, C.-A.; Assimacopoulos, T.; Cuendet, J.-F.; Calanca, A.; Carron, R. Clinique ophtalmologique universitaire, Hopital ophtalmique, 15, avenue de France, CH-1004 Lausanne, Switzerland **/Ophthalmological side-effects of lithium./** Les effets secondaires du lithium en ophtalmologie. Encephale. 7(2):123-128, 1981.

Ophthalmological side-effects of lithium are examined. One of the possible side-effects from psychotropic drugs, especially major tranquilizers, is ocular lesions (opacitus in the cornea and the lens). Ocular examination of 73 patients suffering from affective disorders and receiving lithium salts for several years showed no significant ocular lesions due to the medication. 16 references. (Journal abstract modified)

004616 Hollister, Leo E. Stanford University School of Medicine, Stanford, CA 94305 **Treatment of tardive dyskinesia.** Current Psychiatric Therapies. 19:89-97, 1980.

Tardive dyskinesia is considered in relation to clinical manifestations, prevalance, predisposing factors, differential diagnosis, pathogenesis, treatment, and prevention. Clinical manifestations are repetitive, involuntary, choreoathetoid movements that involve the mouth, lips, tongue, trunk, and extremities, which are not often evident until the patient has been treated for months or years with antipsychotic drugs. Two major modes of treatment become evident if the pathogenesis of tardive dyskinesia is viewed as presenting an imbalance between the dopaminergic and cholinergic systems in the striatum. One mode would be to reduce dopaminergic transmission and the other would be to increase cholinergic transmission. One might also try to increase GABAergic transmission. It is suggested that the uncertain outcome of tardive dyskinesia differs from the usual type of unwanted effect of a drug. 17 references.

004617 Hudson, Charles J. Dept. of Psychiatry, Mary Imogene Bassett Hospital, Cooperstown, NY 13326 **Tricyclic antidepressants and alcoholic blackouts.** Journal of Nervous and Mental Disease. 169(6):381-382, 1981.

Three brief case histories are presented of female patients who experienced blackouts after consuming alcohol, approximately 1 month after starting tricyclic antidepressants. Possible mechanisms for this interactive effect are considered with reference to the central cholinergic activity of tricyclic antidepressants and the increased blood-brain barrier permeability to alcohol found in previous animal research. 8 references. (Author abstract modified)

004618 Ideshita, Hisato; Morita, Hironori; Yoshinaga, Junji; Sasaki, Takanobu; Hikiji, Akiyoshi. Dept. of Neurology, Hiroshima City Hospital, Hiroshima, Japan **A study on mental symptoms developed during the treatment of Parkinson's disease.** Brain and Nerve. 32(9):941-947, 1980.

Psychological symptoms of hallucinations, delusion, and/or delirious state were studied in Parkinson's disease patients. The symptoms occurred in 23 of 101 patients and tended to be highest in the Ss in their 60's. Hypertension and a history of depression were more frequently observed in Ss with psychological symptoms than in those without these symptoms. A mean daily dose of L-dopa for patients at the onset of psychological symptoms was less than was the mean daily maximum dose of L-dopa for Ss without psychological symptoms. Cases with cerebral atrophy had a tendency to develop psychological symptoms, as did those with an abnormal EEG. Cases with psychological symptoms were more often complicated by dyskinesia than were those without these symptoms. It is concluded that the incidence of psychological symptoms during the treatment of Parkison's disease is high in elderly patients who have experienced all or some of the following conditions: psychiatric illness, hypertension, cerebral atrophy, and abnormal EEG. 11 references. (Journal abstract modified)

004619 Itil, T. M.; Herkert, E.; Schneider, S. J.; Luhar, J.; Fredrickson, J. W.; Roffman, M. V.A. Medical Center, Montrose, NY **Baclofen in the treatment of tardive dyskinesia: open label study.** Acta Therapeutica. 6:315-323, 1980.

The effect of baclofen, a GABA derivative, was investigated in a group of schizophrenic patients with the distinct symptoms of tardive dyskinesia. Study was open without control compounds. In some patients, an obvious decrease in dyskinetic movements was observed. No effects of baclofen on psychopathology were noticed. 19 references. (Author abstract)

004620 Itil, Turan M.; Fredrickson, John W.; Schneider, Sid J.; Francis, Irene B.; Khan, Muzaffar M. F.D.R. V.A. Medical Center, Montrose, NY **Clopipazan (SKF-69634), a new neuroleptic essentially free of extrapyramidal liability: quantitative pharmaco-EEG and open label clinical trial.** Current Therapeutic Research. 27(5):719-730, 1980.

The results of a phase I single rising dose tolerance study of clopipazan (SKF-69634) with quantitative pharmaco-EEG (QPEEG) and an early phase II open pilot study are presented. QPEEG analyses revealed that it has systematic effects on human brain function in doses as low as 10mg. These QPEEG effects resembled those of known neuroleptics, but with less rapid onset and longer lasting effects. These results suggested that the compound should have neuroleptic properties, and accordingly it was tested in an uncontrolled, open label early phase II study with a group of hospitalized schizophrenics. Clopipazan was found to be a neuroleptic for some patients, without producing extrapyramidal side-effects. Tardive dyskinesia, present in some patients before treatment, improved slightly. No significant adverse reactions were observed. The potency and onset of the antipsychotic effect of clopipazan, however, was not as strong or as early as with some known neuroleptics. 13 references. (Author abstract modified)

004621 Izrael', Ye. N. Klinika ekzogenno-organicheskikh psikhozov, Moskovskiy NII psikhiatrii, Ministerstvo zdravookhraneniya RSFSR, Moskva, USSR **/Mental disturbances in chronic manganese poisoning./** Psikhicheskiye narusheniya pri khronicheskoy margantsevoy intoksikatsii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(2):105-108, 1981.

Mental disturbances were studied in 35 patients with chronic manganese poisoning, who were examined between 1939 and 1956 in connection with occupational safety. The Ss were 21 men and 14 women (30 to 45 years old) who had been exposed to industrial pollution for periods ranging from less than 1 year to more than 20 years. The worst cases were those of workers who were involved in the processing of manganese ore, and who came into direct contact with manganese dust, the concentration of which was more than 10 times higher than permissible levels. The first symptoms of the disease appeared about 5 to 10 years after the first exposure. These were asthenia, followed by the development of extrapyramidal symptoms. Results show that chronic manganese poisoning led to permanent mental deficiency due to organic brain damage. 5 references. (Journal abstract modified)

004622 Jacquot, M.; Bottari, R. Hopital Sainte-Anne, 1, rue Cabanis, F-75014 Paris, France **/Manic state induced by salbutamol taken orally./** Etat maniaque ayant ete declenche par la prise orale de salbutamol. Encephale. 7(1):45-49, 1981.

A manic state induced by salbutamol taken orally is discussed. A 25-year-old man with no previous psychiatric history, but whose family had several cases of manic-depressive psychosis, exhibited typical manic symptoms after taking salbutamol, which had been prescribed for an asthmatic condition. Salbutamol is known to have a clear and intense action on the mood of endogenous psychotic depressive patients. It is suggested that a manic state can be induced by ingestion of salbutamol. 20 references. (Journal abstract modified)

004623 Jellinek, Theodore; Gardos, George; Cole, Jonathan O. Community Treatment Program, Herbert Lipton Community Mental Health Center, Nichols Rd., Fitchburg, MA 01420 **Adverse effects of antiparkinson drug withdrawal. (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-32675, 1980. 20 p.

The behavioral, affective, and neurological effects of antiparkinson drug discontinuation in schizophrenic outpatients were investigated in a double-blind controlled study. Ss were evaluated at baseline and at 2 and 4 weeks. Nine of the 24 placebo patients terminated early because of adverse effects, while none of the eight controls did so. The placebo group demonstrated statistically significant increases at 2 weeks in lower extremity movement, motor agitation, hallucinations, and physical complaints. At 4 weeks, the placebo group scored significantly higher in depression. It is concluded that a sizeable proportion of chronic drug treated schizophrenics need antiparkinson drug treatment for clinical stability. 31 references. (Author abstract modified)

004624 Johnson, G. F. S. Dept. of Psychiatry, University of Sydney, Sydney, New South Wales, Australia 2006 **Tardive dyskinesia.** Australian and New Zealand Journal of Psychiatry. 14(4):261-263, 1980.

Tardive dyskinesia is discussed in terms of its symptoms, epidemiology, course, treatment, and prevention. The diagnosis of tardive dyskinesia depends on the presence of characteristic movements in a patient with a history of drug exposure. All the antipsychotic drugs may produce this syndrome and the duration of therapy appears critical with a minimum of 6 to 12 months required to produce abnormal movements. The incidence of tardive dyskinesia in patients varies from .5% to 40% depending on differences in definition of the syndrome, population studies, and neurological assessment techniques. Tardive dyskinesia, unlike other extrapyramidal symptoms, may be irreversible and there is no satisfactory treatment once it is established. Prevention is the only effective way of reducing the frequency of tardive dyskinesia. 8 references.

004625 Kiljan, Anna; Pietruszewska, Irena. Klinika Psychiatryczna AM, ul. Nowowiejska 27, 00-665 Warszawa, Poland / **Unwanted effects of lithium carbonate used in the prevention of relapses of affective illness.**/ Niepozadane dzialanie weglanu litu stosowanego w zapobieganiu nawrotom chorob afektywnych. Psychiatria Polska. 14(4):343-350, 1980.

Adverse lithium effects were analyzed in 83 outpatients (42 men and 41 women) who had been treated from 1968 to 1978. Of the patients receiving lithium carbonate, 50 were suffering from bipolar affective illness, 6 from unipolar affective illness, and 27 from schizoaffective psychosis. Adverse symptoms were observed in 25 subjects (30.12%). In six of these patients (1.26%) lithium administration had to be discontinued. It is concluded that lithium carbonate at doses stabilizing serum lithium concentration (approximately 0.7 eE/liter) is relatively well tolerated. Unwanted lithium effects occur more often in women than in men, and initiation of lithium therapy in women ages 50 to 55 years often brings about adverse effects. It has also been found that lithium combined with psychotropic drugs increases the likeliness of the occurrence of unwanted lithium effects. 20 references. (Journal abstract modified)

004626 Kinze, Wolfram; Prohl, Lothar; Brauer, Harald. Kinderneuropsychiatrische Abteilung, Bezirksfachkrankenhaus, Luckauer Strasse 17, DDR-7550 Lubben, German Democratic Republic /**On the question of parenchymal damage caused by long-term therapy with psychotropics in adolescence.**/ Zur Frage der Parenchymschaden durch langfristige Therapie mit Psychopharmaka im Jugendalter. Psychiatrie, Neurologie und Medizinische Psychologie. 32(12):716-722, 1980.

Parenchymal damage caused by long-term pharmcotherapy with psychotropic drugs in adolescents is examined. For 341 patients treated with psychotropic drugs over different time periods and with different dosages, laboratory tests were conducted to determine possible toxic effects and damage to the parenchyma of the liver, the kidneys, and the blood formation systems. Statistically determined differences in some liver functions and in the serum creatinine between treated and untreated patients were found, but no significant indication of direct toxic damage was evidenced. These deviations are considered to be of an allergic nature and to be caused by enzyme induction. 23 references. (Journal abstract modified)

004627 Kocher, R.; Hobi, V.; Linder, M.; Studer, K. Psychiatrische Universitatsklinik, Wilh.-Klein-Strasse 27, CH-4025 Basel, Switzerland /**On the therapy of neuroleptic induced tardive dyskinesia with dimethylaminoethanol (Deanol).**/ Zur therapie mit Dimethylaminoathanol (Deanol) bei neuroleptikainduzierten Spatdyskinesien. Schweizer Arhive fur Neurologie, Neurochirurgie und Psychiatrie. 126(1):103-109, 1980.

A double-blind cross-over study of 20 patients with tardive dyskinesia due to chronic use of neuroleptics showed no difference between efficacy of dimethylaminoethanol (Deanol, Deaner) and placebo. Several patients improved with dimethylaminoethanol, whereas several other patients showed increasing dyskinesia. The same phenomenon could be observed in the placebo group. Tolerance of the compound was very good. Results of an additional open study, however, suggest that the administration of dimethylaminoethanol may be tried so long as no other means are available to define those patients who will react favorably to this medication. 13 references. (Author abstract)

004628 Kuran, Wlodzimierz. Instytut Psychoneurologiczny, Sobieskiego 1/9, 02-957 Warszawa, Poland /**Contemporary problems in the pharmacological treatment of parkinsonism.**/ Wspolczesne problemy farmakologicznego leczenia parkinsonizmu. Neurologia i Neurochirurgia Polska. 14(4):427-435, 1980.

Contemporary problems in the pharmacological treatment of parkinsonism are discussed. The aim of the study was to establish the pathomechanism emerging as side-effects in levodopamine treatment and the introduction of drugs modifying or substituting levodopamine action in the treatment of parkinsonism. Dyskinesis appears as a side-effect in 40% to 65% of the cases treated with levodopamine. Several hypotheses suggest that dyskinesis results from the disturbance of neurotransmitters such as in the GABA system the serotonergic system, or cholinergic activity. A discussion of drugs used to counteract levodopamine side-effects suggests that levodopamine should not be used in cases with minimal symptoms. In these cases anticholinergic or amantadine drugs should be used, and levodopamine should be reserved for cases where the syndrome is strongly developed and very severe. 36 references.

004629 Kuran, Wlodzimierz. Klinika Diagnostyki i Terapii Chorob Neurologiczynch, Al. Sobieskiego 1/9, 02-957 Warszawa, Poland /**Present attempts at treating tardive dyskinesia.**/ Wspolczesne proby leczenia poznych dyskinez. Psychiatria Polska. 14(6):627-633, 1980.

A survey of literature on the present day attempts at treating tardive dyskinesia focuses on the fact that the etiology of the condition has not been clearly established. Several hypotheses are discussed on the pathomechanism of tardive dyskinesia explaining the condition as a dynamic disturbance of the balance of neurotransmitters, particularly those in striation. Approaches to treating the condition are discussed focusing on removing neuroleptics from treatment depending on the mental condition of the patient, substituting neuroleptics blocking dopaminergic receptors, prescribing drugs with an antagonistic effect in relation to dopamine, prescribing cholinergic drugs, drugs with GABAergic activity, agonistic dopamines, and drugs with anticholinergic action. An early diagnosis of the condition is encouraged in order to increase the chances of spontaneous remission. 40 references.

004630 Law, William, III; Petti, Theodore A.; Kazdin, Alan E. Petti: Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Withdrawal symptoms after graduated cessation of imipramine in children.** American Journal of Psychiatry. 138(5):647-650, 1981.

In a systematic retrospective study, the charts of 22 depressed children on a clinical research unit were reviewed following withdrawal from high dose imipramine treatment. Significant withdrawal symptoms were found over seven symptom categories despite an average tapering period of 6.4 days. These results suggest that withdrawal symptoms in children may be much more prevalent and intense than previously recognized. 22 references. (Author abstract modified)

004631 Lawrence, R. C.; Lovering, E. G.; Poirier, M. A.; Watson, J. R. Lovering: Drug Research Laboratories, Health Protection Branch, Tunney's Pasture, Ottawa, Ontario K1A 0L2, Canada **Impurities in drugs V: meprobamate.** Journal of Pharmaceutical Sciences. 69(12):1444-1445, 1980.

One lot of meprobamate raw material and 28 lots of tablets were examined for impurities by thin layer chromatography (TLC). All lots contained di-(2-methyl-2-propyl-3-carbamoyloxypropyl) carbonate at levels that ranged between 0.1 and 1.0% of the total drug content. Nine lots also contained low levels of a second impurity (about 0.1%), and one lot also contained a third impurity (about 0.1%). Estimates of the two unidentified impurities were based on the assumption of a TLC response with furfural/hydrochloric acid spray equivalent to that of meprobamate. 7 references. (Author abstract modified)

004632 Lechat, P.; Lagier, G.; Rouveix, B.; Fontagne, J.; Vincens, M. 15, Rue de l'Ecole-de-Medecine, F-75006 Paris, France **/Undesirable effects of medicines: a review of several publications issued from 1977-1979./** Effets indesirables des medicaments: releve de quelques publications parues en 1977-1979. Therapie. 35(4):483-517, 1980.

Undesirable side-effects of various medicines as evidenced in studies published from 1977-79 are reviewed. The first part of the article concerns known undesirable effects, and includes neuropsychological effects of amantadine, bismuth, chloral hydrate and cimetidine effects on the skin and blood; effects on the heart and blood pressure; and digestive, metabolic, and endocrinal effects. Dangerous combinations also are mentioned: tricyclic antidepressants combined with monoamine oxidase inhibitors; diazepam and tricyclic antidepressants; triacetyloleandomycin and estroprogestatives; and sodium valproate with antiepileptic drugs. Undersirable effects that seem to have appeared in the literature for the first time are cited; these include neuropsychological effects in migraine sufferers using aspirin. A list of products cited is included.

004633 Litvinova, N. M.; Bobritskaya, Z. M.; Gordiyenko, Zh. P.; Gorbatko, L. G. Khar'kovskiy NII nevrologii i psikhiatrii, Khar'kov, USSR **/Pathophysiological and morphological changes in the CNS during long-term administration of haloperidol./** Patofiziologicheskiye i morfologicheskiye izmeneniya v tsentral'noy nervnoy sisteme pri dlitel'nom vvedenii galoperidola. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 81(2):98-102, 1981.

Pathophysiological and morphological changes in the CNS during long-term administration of haloperidol were studied in white rats in relation to the capacity to develop conditioned reflex connections. The 79 animals were divided into 5 groups. Groups 1, 2 and 3 were given haloperidol (1mg/kg per day) for 3, 6, and 9 months respectively. Group 4 received increasing dosages (1 to 12mg/kg) during the course of a month until the appearance of extrapyramidal disorders. Group 5 was a control group. Motor defensive conditioned avoidance reflexes were developed, and the animals were then decapitated. Sections of the sensorimotor cortex and caudate nucleus (7mcm thick) were examined. Results show that in groups 1, 2, and 3 haloperidol caused function adaptive, dystrophical, and compensatory changes in the cytoplasm, nuclei, nucleoli, neurons, and glial cells of the somatosensory zone of the cortex and subcortical nodes. In group 4 haloperidol caused CNS damage and changed forms of compensation. Haloperidol did not significantly affect the cortical function of the formation of conditioned reflexes, but after 6 months it retarded the fixation of new conditioned reflexes. 7 references. (Journal abstract modified)

004634 Maksimowska, Maria. II Klinika Psychiatrii SL. AM, ul. Pyskowicka, 42-690 Tarnowskie Gory, Poland **/An unusual case of thioridazine and levomepromazine dependence./** Szczegolny pryzypadek uzaleznienia od tiorydazyny i tisercyny. Psychiatria Polska. 14(5):547-548, 1980.

An unusual case of thioridazine and levomepromazine dependence is described. The 49-year-old S reported to the clinic complaining of insomnia and oversensitivity. He had used thioridazine and levomepromazine for more than 1.5 years and also took 3 tablets of Pfeiffer's substance every other day. Although addiction to these drugs has not been noted, it must be taken into account when prescribing them, particularly to alcoholics and drug addicts. 7 references.

004635 Marriott, Peter; Pansa, Monika; Hiep, Albert. Melbourne Clinic, PO Box 194, Richmond 3121, Australia **Depot fluphenazine maintenance treatment and associated weight changes.** Comprehensive Psychiatry. 22(3):320-325, 1981.

The relationship between depot fluphenazine maintenance treatment and weight change was examined in 110 patients remaining on fluphenazine decanoate for 2 years of continuous treatment at the Melbourne Depot Neuroleptic Clinic. It was found that 74.5% of all patients maintained a stable weight, 14.5% gained over 3 pounds, and 10.9% decreased their weight by more than 3 pounds. It was not possible to demonstrate a relationship between weight gain and time in treatment or dosage level. Both antiparkinsonian and tricyclic antidepressant drugs may play a role in weight change: 42% of Ss in the weight loss group were prescribed antidepressants, as compared to 13% and 17% in the weight gain and no change group, respectively; almost all those in the weight gain group (94%) had been prescribed antiparkinsonian drugs at some point during the study, as compared to 58% and 61% of the weight loss and stable groups 12 references.

004636 Matsunaga, Fumiyasu; Akiyama, Akinori; Fujii, Isao. Health Service Center of Nagasaki University, Nagasaki City, Japan **Two cases of levels of serum CPK.** Kyushu Neuro-Psychiatry. 26(2):274-280, 1980.

Two cases of syndrome malin with high levels of serum creatine phosphokinase (CPK) were studied. The first case was a 28-year-old depressed female patient who was rushed to the hospital after taking 200mg of levomepromazine and 450mg of flurazepam in a suicide attempt. On her third day at the hospital the i.m. administration of chlorpromazine (50mg) caused a fever of 37.8 degrees C., sweating, finger tremor, and rigidity. Syndrome malin was suspected. The second case was a 32-year-old male who had received chlorpromazine for 1 day for catatonic schizophrenia. When chlorpromazine (170mg) was replaced by oxypertine (240mg) and pimozide (3mg), he suffered from hyperpyrexia, sweating, and rigidity. In both cases the condition improved when the drugs were discontinued and intravenous infusion was given. It is concluded that the early detection of prodromal symptoms and elevated serum CPK will help prevent syndrome malin caused by neuroleptics. 20 references. (Author abstract modified)

004637 Mattsson, Ake; Seltzer, Ronni L. Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New

York, NY 10016 **MAOI-induced rapid cycling bipolar affective disorder in an adolescent.** American Journal of Psychiatry. 138(5):677-679, 1981.

The likely inducement of a rapid cycling bipolar disorder in an adolescent treated with a monoamine oxidase inhibitor (MAOI) for unipolar depression is reported. The case report strongly suggests such an inducement in Ss prone to affective illness due to pubertal (biological as well as adolescent reactive) factors. The symptoms seemed to be preciptated by administration of phenelzine and lithium carbonate proved effective in preventing further cycling after about 5 weeks of administration. The clinical characteristics are consistent with findings of rapid affective cycling induced by tricyclic antidepressants in five women. 8 references.

004638 Mauguiere, F.; Dalery, J.; de Villard, R.; Courjon, J. Service d'electroencephalographie, Hopital neurologique, 59, boulevard Pinal, F-69003 Lyon, France **Transient hyperkinesia after a single intravenous perfusion of diphenylhydantoin: report of a case associated with nontoxic plasma levels of diphenylhydantoin.** European Neurology. 18(2):116-123, 1979.

Transient hyperkinesia was observed in a 16-year-old epileptic, mentally retarded boy after a single i.v. perfusion of diphenylhydantoin (DPH). Serum DPH levels were not in the toxic range, and the usual symptoms of DPH intoxication (nystagmus and cerebellar dysfunction) were not present. Neuroradiological examination revealed no anatomical damage to the basal ganglia. Homovanillic acid (HVA) concentration in the cerebrospinal fluid was low, but 5-hydroxyindoleacetic acid (5-HIAA) concentration was normal 6 hours after the onset of choreothetosis. Both metabolites were within normal range 2 months later. Results are discussed in relation to cerebral monoamine metabolism in drug treated epileptic patients. 19 references. (Author abstract modified)

004639 McIntyre, Iain M.; Burrows, Graham D.; Norman, Trevor R.; Dumovic, Peter; Vohra, Jitu. Dept. of Psychiatry, University of Melbourne, Melbourne, Australia **Plasma nomifensine concentration: cardiological effects and clinical response.** International Pharmacopsychiatry. 15(6):325-333, 1980.

Cardiological effects of nomifensine were studied in 10 endogenously depressed inpatients receiving up to 200mg/day for 3 weeks. No significant cardiac effects were observed using His' bundle electrography and electrocardiography. Nine of the 10 patients showed a significant recovery from their depressive illness. Plasma nomifensine concentrations at day 22 were not correlated with clinical response, blood pressure, or electrocardiographic parameters. A negative correlation between A-H interval in the His' bundle electrogram and day 22 nomifensine concentration was observed. 25 references. (Author abstract)

004640 Mendis, N.; Pare, C. M. B.; Sandler, M.; Glover, Vivette; Stern, G. M. Sandler: Bernhard Baron Memorial Research Lab., Queen Charlotte's Maternity Hospital, London W6 OXG, England **Is the failure of (-)deprenyl, a selective monoamine oxidase B inhibitor, to alleviate depression related to freedom from the cheese effect?** Psychopharmacology. 73(1):87-90, 1981.

The selective monoamine oxidase (MAO) B inhibitor (-)deprenyl failed to produce any greater benefit than placebo in a limited double-blind trial conducted in depressive patients. Its relative freedom from the so called cheese effect was confirmed, however, in drug treated patients challenged IV with tyramine. There is evidence to suggest that this cheese effect, a facilitated tyramine-induced hypertensive response, is pharmacologically distinct from MAO inhibition proper. Thus, it is conceivable that its central counterpart, an enhanced noradrenaline release due to the access of traces of tyramine to the CNS, is a prerequisite for any therapeutic benefit obtainable with the MAO inhibitory drugs in general. 40 references. (Author abstract)

004641 Moore, David P. Dept. of Psychiatry, University of Louisville, Box 35070, Louisville, KY 40232 **A case of petit mal epilepsy aggravated by lithium.** American Journal of Psychiatry. 138(5):690-691, 1981.

A case report on the effect of lithium on the frequency of petit mal seizures is presented and the relevant literature is briefly reviewed. The case history demonstrates that lithium may dramatically increase such seizures and that it should be carefully monitored on an inpatient basis when given to an epileptic patient with an affective disorder. 6 references.

004642 Nachtman, V.; Nosek, I.; Polacek, J. Interni oddeleni nemocnice OUNZ, 509 01 Nova Paka, Czechoslovakia **/A case of acute agranulocytosis during treatment with clozapine./** Pripad akutni agranulocytozy v prubehu lecby clozapinem. Ceskoslovenska Psychiatrie. 76(6):393-398, 1980.

The case of a 47-year-old patient suffering from paranoid schizophrenia in whom the syndrome of acute agranulocytosis appeared after treatment with clozapine (Leponex) is considered. The syndrome appeared on the 26th day after administration of 8.75g of clozapine. The patient was being treated by other psychotherapeutic drugs as well, although no complications had occurred in the past. After the interruption of psychotherapeutic treatment on the 38th day of hospitalization, a decrease in neutrophils still continued, so that the lowest number was found on the 44th day of hospitalization. Normalization was achieved on the 51st day of hospitalization (10th day after the administration of prednisone). The need for regular blood analysis, which is the prerequisite for decreasing mortality from this serious complication, is emphasized. 4 references. (Journal abstract modified)

004643 Nagy, Brian R.; Dillman, Carl E., Jr. Elmira Medical Arts Center, Elmira, NY 14901 **Case report of unusual diazepam abstinence syndrome.** American Journal of Psychiatry. 138(5):694-695, 1981.

A case study is presented of the unusual diazepam abstinence syndrome, in which the diagnosis clearly seemed to be diazepam withdrawal but the symptoms lasted an extended period of time (30 days). The patient also initially became sleepy when diazepam was given rather than having a clearer sensorium, and the symptoms showed no clear cross-tolerance with pentobarbital. The findings should facilitate earlier diagnosis of this syndrome and may encourage drug therapy that is appropriate and adequate in dosage. 10 references.

004644 Olajossy, Marcin. Klinika Psychiatrii, Akademia Medyczna, Abramowicka 2, 20-442 Lublin, Poland **/Tardive dyskinesia: problems of pathogenesis, therapy, and prevention./** Pozne diskinezy: zagadnienia patogenezy, leczenia i zapobiegania. Psychiatria Polska. 14(6):621-625, 1980.

A survey of literature on the pathogenesis, therapy, and prevention of tardive dyskinesia focuses on its emergence during the prescription of high doses of neuroleptics. In addition the effect is also noted in cases of long-term treatment with L-dopa. It has been noted that a decisive majority of tardive dyskinesia cases are associated with schizophrenia. Among the factors that serve as determinants seem to be sex (women appear to be more susceptible), age (particularly after the age of 60), the dosage of the drug, the extent of organic damage, and changes in EEG readings. A prognosis is unavailable due to lack of objective data on tardive dyskinesia; however, it is suggested that patients should be carefully controlled with the emergence of the first symptoms. 30 references.

004645 Orr, Martha Lane. Rogosin Kidney Center, New York Hospital, New York, NY 10021 **Drugs and renal disease.** American Journal of Nursing. 81(5):969-971, 1981.

The principles guiding medication use in patients with seriously compromised renal function are discussed. These principles are based primarily on alterations in the absorption, distribution, metabolism, and excretion of drugs, alterations that are either directly or indirectly related to the renal impairment. The aim is to avoid or quickly counteract the toxic side-effects of such drugs as narcotics, barbiturates, and sedatives in uremic patients. Confounding problems include extra sensitivity to drugs among these patients, conflicting therapeutic requirements, and complications of dialysis.

004646 Petrie, William M. Dept. of Psychiatry, Vanderbilt University Medical School, Nashville, TN 37216 **Sexual effects of antidepressants and psychomotor stimulant drugs.** Modern Problems of Pharmacopsychiatry. 15:77-90, 1980.

Research on sexual dysfunction occurring in mental disorders as a result of treatment with antidepressant and stimulant drugs is reviewed. It is reported that such dysfunction is most common in depression and is manifested as a loss of sexual interest, impotence, and a decline in the frequency of intercourse. The antidepressant drugs have been demonstrated to improve sexual function, but to also have adverse effects as a result of interference with peripheral cholinergic and adrenergic function. MAO inhibitors have also been found to ameliorate depression related dysfunction, espcially by improving sperm count and sperm motility and by having a clinical effect in moderate oligospermia. Research on the stimulant drugs has indicated a wide variety of sexual effects, most dramatic of which is the increase in sexual arousal reported by many users. Increases in sexual activity and perversion have also been reported. Due to the high rate of predrug sexual aberration and the nonspecific nature of stimulant arousal, caution is urged in postulating a direct effect on sexuality by these compounds. 62 references.

004647 Reid, William H.; Arkfeld, Dean Francis. Nebraska Psychiatric Institute, 602 South 45th Street, Omaha, NE 68106 **Psychotropic medications and glaucoma.** Hillside Journal of Clinical Psychiatry. 2(2):217-221, 1980.

Studies investigating the relationship between psychotropic drugs and glaucoma are reviewed. The autonomic effects of psychotropics have been related to a potential for precipitating or exacerbating glaucoma. This is particularly true in the case of angle closure glaucoma. It is concluded that antiglaucoma medications and ophthalmological examinations can eliminate problems in almost all cases. 10 references.

004648 Rektor, L.; Blazek, J. PL KUNZ, Huskova 2, 600 00 Brno, Czechoslovakia **/Results of treatment by Modites depot in outpatients' wards in the South Moravian Region./** Vysledky liecby Moditenom depot v ambulanciach Juhomoravskeho kraja. Ceskoslovenska Psychiatrie. 76(6):369-375, 1980.

Results of depot fluphenazine treatment, especially with schizophrenic outpatients, in Czechoslovakia's South Moravian Region, were assessed in 1978. Based on 675 cases, it was found that an average of 40% of the patients returned to work, and there was a decline in relapses and rehospitalizations. The most frequent side-effects were Parkinson's syndrome manifested by akathisia, inhibition, and hypomimic activity. Dyskinesias were rarely observed. It is proposed that the frequent occurrence of extrapyramidal symptomatology is connected with individual tolerance and the added complication of medication with other neuroleptics. Parkinson's syndrome was successfully treated by antiparkinsonian drugs and only rarely required hospitalization or discontinuance of treatment. Prophylactic medication by antiparkinsonian medications is not recommended; however, the need for regular control of the patient by the attending physician or psychiatrist to determine other side-effects or psychotherapeutic or sociotherapeutic complications is noted. It is proposed that outpatient treatment with depot fluphenazine be continued by the Regional Institute of National Health in Brno as part of the psychiatric program. 10 references. (Journal abstract modified)

004649 Reynolds, Edward H. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London, England **Anticonvulsants and mental symptoms.** Acta Neurologica Scandinavica. 62(Suppl. 80):46-52, 1980.

Evidence is reviewed which suggests that anticonvulsant drugs and their various metabolic effects, especially on a long-term basis, contribute significantly to psychological (mental) problems in epileptic patients. The effects of drugs such as phenobarbitone and phenytoin include impairment of drive, mood, concentration, and sociability. Current knowledge concerning mental function in epileptic patients is specifically reviewed in relation to blood levels of the various anticonvulsants and in relation to the metabolic consequences of chronic therapy, particularly folate deficiency, monoamine metabolism, and hormone metabolism. The need for continued research in this neglected field is emphasized. 27 references.

004650 Reynolds, Philip C.; Som, Constance W.; Herrmann, Paul W. Institute of Forensic Sciences, Oakland, CA 94609 **Loxapine fatalities.** Clinical Toxicology. 14(2):181-185, 1979.

Two cases of suicidal ingestion of the antipsychotic drug loxapine are reported. Investigations indicated that one patient may have ingested 2500mg loxapine. In the second patient, 2900mg loxapine were found in the stomach after death. 7 references.

004651 Roffman, M.; Cordasco, F.; Kling, A. Dept. of Psychiatry, CMDNJ-Rutgers Medical School, Piscataway, NJ **Apomorphine-induced stereotypy in mature and senescent rats following cessation of chronic haloperidol treatment.** Communications in Psychopharmacology. 4(4):283-286, 1980.

Apomorphine-induced stereotypy in mature and senescent rats was studied following cessation of chronic haloperidol treatment. After chronic haloperidol treatment, senescent rats exhibited significantly more apomorphine-induced stereotypy than did similar rats chronically treated with saline. The intensity of this stereotypy was less than that exhibited by mature rats that were chronically treated with haloperidol. Similarly, senescent rats chronically treated with saline exhibited less apomorphine-induced stereotypy than mature rats comparably treated. However, after chronic haloperidol, the percent change in stereotypy from respective control was greater for the senescent rats than the mature rats. These data suggest that senescent rats were more sensitive to the effects of chronic antipsychotic treatment than mature rats and support clinical observations of increased sensitivity of tardive dyskinesia in the elderly. 9 references. (Author abstract modified)

004652 Rondot, P.; Bathien, N. Service de Neurologie, Faculte de Medecine Cochin-Port-Royal, Hopital Sainte-Anne, 1, rue Cabanis, Paris 14eme, France **/Abnormal movements induced by psychotropic drugs./** Mouvements anormaux induits par les medicaments psychotropes. Encephale. 5(1):41-48, 1979.

Abnormal movements that are related to various physiopathological mechanisms induced by psychotropic drugs are discussed. Blockage of dopaminergic receptors provokes neuroleptic parkinsonian tremor. Neuroleptic-induced tardive dyskinesia is similar to abnormal movements caused by L-Dopa. However, tardive dyskinesia is due to a hypersensibility of dopaminergic reactors which has a chemical effect on afferent impulses, while L-Dopa dyskinesia is probably related to altered responsiveness of these receptors due to an increase in dopaminergic receptor sensitivity. Antidepressants, particularly lithium, provoke tremor which is improved by beta-blockers; it is probably caused by abnormal sensitivity to beta-noradrenergic receptors. 17 references. (Journal abstract modified)

004653 Ruff, Robert L.; Kutt, Henn; Hafler, David. Dept. of Medicine, Div. of Neurology RG 20, University of Washington, Seattle, WA 98195 **Prolonged benzodiazepine coma.** New York State Journal of Medicine. 81(5):776-777, 1981.

A case of prolonged coma in a 48-year-old woman, following a suicidal overdose of flurazepam and chlordiazepoxide, is described. These agents belong to the benzodiazepines, a widely used class of drugs which rarely cause prolonged coma in drug overdose. The 10 day duration of the coma, the complete loss of cranial nerve reflexes, and the extreme cardiovascular and respiratory depression seen in this case reflect the magnitude of the patient's drug ingestion. The patient completely recovered. The importance of careful medical management of severe sedative-hypnotic overdose is discussed. 8 references. (Author abstract modified)

004654 Schubert, Daniel S. P. Dept. of Psychiatry, Cleveland Metropolitan General Hospital, 3395 Scranton Road, Cleveland, OH 44109 **Hostility production as a common feature of anti-anxiety agent action.** Journal of Psychiatric Treatment and Evaluation. 1(2):43, 1979.

A case is presented in which treatment of imipramine-induced anxiety with hydrozine (25 to 50mg given concomitantly with imipramine, three to four times daily) produced hostility. Hydrozine seems similar to the benzodiazepines in reducing anxiety, and similarly may produce hostility. Limbic cholinergic inhibition may account for the release of hostility found both with the antihistamine, hydrozine, and with some benzodiazepines. Considering the parallel action of these two anxiolytics, anxiety and hostility may reflect the same process in some patients: inward turned hostility may produce anxiety in some individuals and depression in others. The possible contributions of this induced hostility in psychotherapy are noted. 4 references.

004655 Scully, Robert E.; Galdabini, James J.; McNeely, Betty U. Massachusetts, General Hospital, Boston, MA 02114 **/The role of lithium in the production of interstitial nephritis: a case history./** Case 17-1981. New England Journal of Medicine. 304(17):1025-1032, 1981.

The case history of a 29-year-old man on lithium therapy for manic-depressive illness who suffered renal failure is reported. It is concluded that the patient had chronic interstitial nephritis. Although the lithium therapy may have contributed to the renal damage, it is found that the lesion is nonspecific and that a causal agent cannot be defined. Circumstantial evidence, however, suggests that lithium therapy was a factor. The need for careful study of patients on lithium therapy in whom renal insufficiency develops is pointed out. 48 references.

004656 Sethi, B. B.; Prakash, Rudra; Sharma, Mukul; Sahai, J. Dept. of Psychiatry, K. G.'s Medical College, Lucknow, India **Tricyclic anti-depressant induced mania.** Indian Journal of Psychiatry. 22(4):378-383, 1980.

Four cases of monopolar depression are reported in patients who developed manic features for the first time while on tricyclic antidepressant therapy. The phenomenon is viewed as tricyclic antidepressant-induced mania. The manic symptoms occurred late in therapy with moderate doses of tricyclic antidepressants (125 to 150mg per day) and were easily controlled with antipsychotic medication. Factors relating to age of patients, metabolic products of tricyclic an tidepressants, and central noradrenergic and dopaminergic systems are considered important and their role is discussed. 22 references. (Author abstract modified)

004657 Shader, Richard I.; Elkins, Robert. Dept. of Psychiatry, Tufts Medical School, 171 Harrison Ave., Boston, MA 02111 **The effects of antianxiety and antipsychotic drugs on sexual behavior.** Modern Problems of Pharmacopsychiatry. 15:91-110, 1980.

Research on the effects of antianxiety and antipsychotic agents on human sexual behavior is reviewed, and possible mechanisms of action derived from animal studies are discussed. It is reported that little is known about the effects of these drugs on sexual feelings and behavior, and that potential adverse effects, as well as possible treatments, can be suggested. Findings are presented from studies of the manner in which the compounds may influence sexual behavior; effects on the CNS as well as the behavioral pharmacology; and the clinical features of these drugs. Since most of the anxioltyic sedatives prescribed currently are benzodiazepines, this class of minor tranquilizers is emphasized. Some information is also provided on antipsychotic agents such as the phenothiazines and on sedative hypnotics. Topics include the usefulness of the benzodiazepines in the disinhibition of sexual behavior in such conditions as erectile dysfunction; aspermia associated with use of antipsychotic drugs; the neuroleptic-induced Kluver-Bucy syndrome; the use of neuroleptics in treating sex offenders; ejaculatory problems caused by sedative hypnotics and anxiolytic agents; neuroleptic treatment of vaginismus; and systematic drug desensitization in the treatment of frigidity and other mixed sexual dysfunctions. 103 references.

004658 Shaywitz, Sally E.; Cohen, Donald J.; Shaywitz, Bennett A. Learning Disorders Unit, Dept. of Pediatrics, 333 Cedar St., New Haven, CT 06510 **Behavior and learning difficulties in children of normal intelligence born to alcoholic mothers.** Journal of Pediatrics. 96(6):978-982, 1980.

Children referred to a learning disorders unit of a hospital were evaluated for indications of prenatal exposure to ethanol. In a total population of 87 children, 15 were found to have a history of maternal heavy drinking during pregnancy. The 11 boys and 4 girls ranged in age from 6.5 to 18.5 years. Birthweights ranged from 1,580 to 3,150 gm, with a median weight of 2,213 gm. All growth measurements were affected. The children had a continuum of dysmorphic features of fetal alcohol syndrome (FAS), with an inverse relationship between age of presentation and intensity of dysmorphic features. All Ss had intelligence in the average range, yet experienced persistent academic failure. All shared problems of activity and attention regulation. The findings suggest a continuum of teratogenic effects of ethanol on the CNS. It is concluded that alcohol exposure in utero may be an important, preventable determinant of attention deficit syndromes in childhood. 20 references. (Author abstract modified)

004659 Siever, Larry J.; Cohen, Robert M.; Murphy, Dennis L. NIMH, Bldg. 10, Room 3D41, Bethesda, MD 20205 **Antidepressants and alpha2-adrenergic autoreceptor desensitization.** American Journal of Psychiatry. 138(5):681-682, 1981.

The hypothesis that antidepressant treatment alters alpha2-adrenergic responsivity in man was tested by administering clonidine before and after antidepressant medication to two Ss diagnosed as having major depressive illness. A decrease in the magnitude of the clonidine-induced blood pressure fall occurred after chronic, but not acute antidepressant treatment. This finding is the first data in man indicating that clonidine treatment involves a subsensitization of presynaptic alpha2-adrenergic autoreceptors. 9 references.

004660 Sklodwoski, Henryk; Chojnacki, Jan; Gorski, Henryk; Kocur, Jozef. Instytut Higieny Psychicznej WAM, ul. Aleksandrowska 159, 91-229 Lodz, Poland **/An evaluation of the antianxiety action and side-effects of propranolol./** Ocena skutecznosci przeciwlekowej i dzialan ubocznych propranololu. Psychiatria Polska. 14(5):475-480, 1980.

Propranolol was administered to 35 patients with anxiety neurosis and to 10 patients with chronic anxiety due to an underlying condition of encephalopathy to evaluate the efficacy of the drug in anxiety states of various etiology. The patients were subjected to a series of clinical and laboratory examinations aimed at giving the clearest possible objective picture of the dynamics of changes occurring during the morbid process. Propranolol was found to be an effective anxiolytic agent at relatively low dosages, and it also improved intellectual efficiency and memory. Side-effects were mild, infrequent, and easily controlled. 15 references. (Journal abstract modified)

004661 Swartz, Conrad Melton; Holkesvick, Reid. Dept. of Psychiatry, University of Iowa Hospitals and Clinics, 500 Newton Road, Iowa City, IA 52242 **Mitigating acute skin rashes and nausea from lithium.** Comprehensive Psychiatry. 22(3):301-305, 1981.

Five cases are presented in which side-effects of an acute skin reaction (in one patient) and nausea without high blood levels (in four patients) threatened to take precedence over lithium's therapeutic effects. In the first case, the allergic reaction was successfully treated with hydroxyzine. In the remaining cases, patients with nausea related side-effects could be classified as pH sensitive or lithium ion sensitive. Use of lithium citrate syrup giving many small doses, and the use of a sustained release lithium carbonate preparation are possible approaches to the management of nausea related side-effects. 5 references.

004662 Trimble, M. R. National Hospital for Nervous Diseases, Queen Square, London WC1N 3BG, England **New antidepressant drugs and the seizure threshold.** Neuropharmacology. 19(12):1227-1228, 1980.

Studies of the effects of new antidepressant drugs (mianserin, nomifensine, and maprotiline) on seizure threshold are reviewed. The evidence suggests that not all nonmonoamine oxidase inhibitor antidepressants lower the seizure threshold to the same degree. Nomifensine, of the drugs currently available, seems the least likely to do so and early clinical trials in patients with epilepsy suggest it is safe in this condition. 12 references.

004663 Vartanyan, F. Ye.; Gerchikov, L. I. World Health Organization, Geneva, Switzerland **/Side-effects and undesirable combinations of psychotropic medications./** Pobochnyye reaktsii i nezhelatel'nyye kombinatsii psikhotropnykh sredstv. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(2):289-292, 1980.

Side-effects and undesirable combinations of psychotropic medications are discussed. This subject has become more important because of the increased use of medications, sometimes without sufficient medical guidance and control. Undesirable side-effects include: general organic disorders, skin disorders, gastrointestinal disorders, functional disturbances of the CNS and peripheral nervous system, and mental disorders. The topics discussed include: changes in blood pH, disturbances of metabolism from medications, disturbances of urine excretion from medications, and biologically active compounds which have psychotropic properties when used in small doses. 20 references.

004664 Wahlin, Anders; Bucht, G.; von Knorring, L.; Smigan, L. Dept. of Internal Medicine, University Hospital of Umea, S-901 85 Umea, Sweden **Kidney function in patients with affective disorders with and without lithium therapy.** International Pharmacopsychiatry. 15(4):253-259, 1980.

The ability to concentrate urine was estimated in healthy volunteers, patients with affective disorders who had never received lithium, and lithium treated patients. Patients with affective disorders who had never received lithium were found to have significantly lower concentrating capacity than healthy volunteers. However, lithium treated patients had still lower concentrating capacity and differed significantly from both healthy volunteers and from patients who had never received lithium. Furthermore, in a subgroup of lithium treated patients investigated twice with an interval of 6 months, a progressive decrease in concentrating capacity was found, indicating the importance of lithium therapy. 11 references. (Author abstract)

004665 Walker, Sandra; Yesavage, Jerome A.; Tinklenberg, Jared R. Yesavage: V.A. Medical Center, Palo Alto, CA 94304 **Acute phencyclidine (PCP) intoxication: quantitative urine levels and clinical management.** American Journal of Psychiatry. 138(5):674-675, 1981.

Retrospective data are presented on the management of 100 patients with phencyclidine (PCP) intoxication (DSM-III category 305.9), and the relationships between such intoxication and the patients' quantitative urine levels of PCP are discussed. The use of diazepam did not prolong PCP intoxication and the findings suggest that neuroleptic and diazepam treatments are safe, although there is the possibility of rare drug interactions. The quantitative urine PCP levels did not provide clinically useful data beyond that which could be obtained from a qualitative measure. 5 references.

004666 Weiss, B. School of Medicine and Dentistry, Rochester University, Rochester, NY 14627 **Microproperties of operant behavior as aspects of toxicity.** Springfield, VA, NTIS, UR-3490-1877, 1980. 16 p.

The role and utility of perturbations in operant behavior as an assay system in the fields of pharmacology and toxicology are described. (Author abstract modified)

004667 Woggon, Brigitte. Psychiatrische Universitatsklinik, Forschungsabteilung, Postfach 68, CH-8029 Zurich, Switzerland **/Development of psychopharmacology./** Entwicklungen der Psychopharmakotherapie. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie. 125(2):271-285, 1979.

Based on experiences during long-term treatment with psychotropic drugs, the following subjects are discussed: extrapyramidal side-effects of neuroleptic drugs, cardiovascular side-effects of antidepressants, side-effects of lithium, interactions with other medications, influence on laboratory tests, and psychopharmacological treatment during pregnancy. 46 references. (Journal abstract)

004668 Yassa, R.; Ananth, J. Douglas Hospital Centre, 6875 LaSalle Boulevard, Verdun, Quebec H4H 1R3, Canada **Lithium carbonate in the treatment of movement disorders. A critical review.** International Pharmacopsychiatry. 15(5):301-308, 1980.

The efficacy of lithium therapy in the treatment of tardive dyskinesia is reviewed. It is noted that most of the published papers on this topic are anecdotal and single case reports with contradictory results. The well designed studies indicate that lithium is useful in certain tardive dyskinesia patients and that the red blood cell lithium level may be related to the therapeutic response. Therefore, on the basis of the available information, it is concluded that routine clinical application of lithium in the treatment of tardive dyskinesia is not warranted. However, further evaluation of lithium in the treatment of tardive dyskinesia and identification of the responders are extremely useful. In addition, as suggested by animal studies, the prophylactic value of this agent against tardive dyskinesia is seen as needing exploration. 32 references. (Author abstract)

16 METHODS DEVELOPMENT

004669 Ashton, H.; Marsh, V. R.; Millman, J. E.; Rawlins, M. D.; Telford, R.; Thompson, J. W. Clinical Psychopharmacology Unit, Dept. of Pharmacological Sciences, University of Newcastle-upon-Tyne, Newcastle-upon-Tyne, England **The use of event-related slow potentials of the brain as an objective method to study the effects of centrally acting drugs.** In: Barber, C., Evoked potentials. Baltimore, MD, University Park Press, 1980. 614 p. (p. 535-538).

Evidence is presented to show that the event related slow potential (contingent negative variation, CNV) can be used as an objective test for measuring the effects of drugs on brain activity in man. The CNV is believed to be a measure of attention or arousal and is altered by a number of centrally acting drugs. The size of the CNV is consistently increased by stimulant drugs, for example, caffeine and pemoline, and decreased by depressant drugs, for example. nitrazepam and diazepam, in small doses which do not produce subjective effects. Cigarette smoking may increase or decrease the size of the CNV, or sometimes both. Nicotine has a biphasic dose related effect on the CNV. The CNV can be used as a sensitive, reproducible, quantitative, and objective test for studying the central effects of drugs in man and it is suggested that this method is a useful addition to those already available for the study of psychotropic drugs in animals and man. 10 references.

004670 Bress, William; Ziminski, Kenneth; Long, Walter; Manning, Thomas; Lukash, Leslie. Nassau County Medical Examiners Office, East Meadow, NY 11554 **Separation of barbiturates using reverse-phase thin-layer chromatography.** Clinical Toxicology. 16(2):219-221, 1980.

A procedure for separating barbiturates by reverse phase thin layer chromatography (TLC) is described. A spotted TLC plate is dipped in mineral oil/petroleum ether and run 15cm in a solvent of water, methanol, and ammonium hydroxide. After visualization, the drugs tested showed distinct separation. 10 references.

004671 Bridge, T. Peter; Rosenblatt, Jack E.; Burbach, Rodney V.; Wyatt, Richard Jed. Adult Psychiatry Branch, Division of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Saliva benzodiazepine levels and clinical outcome in detoxifying alcoholic patients.** Communications in Psychopharmacology. 4(5):357-361, 1980.

Initial application of a recently developed saliva benzodiazepine radioreceptor assay was completed in a group (n=18) of detoxifying alcoholic patients who were treated with benzodiazepines. All patients were evaluated clinically by their treating psychiatrist at the initiation and completion of benzodiazepine treatment. Saliva benzodiazepine concentrations appeared to discriminate treatment responders from nonresponders in this sample. When separated into responder and nonresponder groups based on change of psychopathology scores, the two groups have differences in amount of benzodiazepine present in
saliva as well as divergent relationships of psychop
scores, benzodiazepine saliva, and benzodiazepine dosag
erences. (Author abstract modified)

004672 Budd, Robert D.; Walkin, Elisabeth. Ran
Amigos Hospital, Downey, CA 90242 **Mass screening**
firmation of diazepam in urine by EMIT-thin-layer c
graphy. Clinical Toxicology. 16(2):201-207, 1980.

A rapid, sensitive, and specific procedure is desc
mass screening and confirmation of diazepam in urine
as low as 0.5mcg/mL. Raw urine specimens are screene
ly by the enzyme multiplied immunoassay technique,
tive samples are confirmed by thin layer chromatograp
zepam and its metabolites are converted to benzopheno
zepam, 3-hydroxydiazepam, and its glucuronide yield 2-
mino-5-chlorobenzophenone (MACB); whereas n-desm
zepam, oxazepam, and oxazepam glucuronide yield 2-
chlorobenzophenone (ACB). The two benzophenones
separated by a solvent system of petroleum ether/glaci
acid and can be detected under ultraviolet light. A spec
ported positive for diazepam must produce spots for b
and MACB. 11 references. (Author abstract modified)

004673 Burke, D.; Sokoloff, H. Sokoloff: Quality
Dept., Hoffman-La Roche Inc., Nutley, NJ 07110 **Sim**
high-performance liquid chromatographic determination
diazepoxide and amitriptyline hydrochloride in two-c
tablet formulations. Journal of Pharmaceutical
69(2);138-140, 1980.

A rapid, precise, and accurate high-performance liq
matographic procedure was developed for simultaneo
mination of amitriptyline hydrochloride and chlordiaze
two component tablet formulations. The impurities and
position products of both components were separated,
the determination specific for amitriptyline hydrochlo
chlordiazepoxide. The method was used for the assay,
uniformity, and dissolution testing of dosage forms con
to 30mg chlordiazepoxide and 12.5 to 75mg of amitrip
references. (Author abstract modified)

004674 Carroll, Bernard J.; Mukhopadhyay, Sunil;
Michael. Clinical Studies Unit, Mental Health Resear
tute, Dept. of Psychiatry, University of Michigan, An
MI 48109 **Radioimmunoassay of tricyclic antidepress**
search Report, NIMH Grant 5R01-MH-28294, 1980. 14

The radioimmunoassay (RIA) techniques described b
wick et al (1978) for measuring plasma concentrations
clic antidepressant (TCA) drugs was evaluated. The th
steps in the method are outlined, along with results in
of procedures for antidbody use and RIA quantitatio
were cited on the validity of the assay, along with fin
alpha-1 acid glycoprotein concentrations. The results
excellent recovery and separation of tertiary and s
amine TCA compounds by solvent extraction. The
and precision of the assay were very good across a wi
of TCA concentrations, and the values found by RIA
closely with those obtained by gas liquid chromat
Overall, the RIA method is seen as having many advan
the quantitation of plasma (TCA) concentrations by sma
tal laboratories. 6 references.

004675 Corona, G. L.; Zerbi, F.; Pinelli, P.; Fenoglio,
tini, P.; Cucchi, M. L.; Santagostino, G. University
Pharmacology, School of Pharmacy, I-27100 Pavia, It
triptyline and nortriptyline plasma levels monitoring. Pe
in clinical practice. Communications in Psychopharm
4(4):309-316, 1980.

One hundred and twenty depressed female inpatients, treated intramuscularly by different amitriptyline dosages, were studied to show the relationship between the plasma levels of amitriptyline and its metabolite nortriptyline, side-effects, and clinical responses. Data were analyzed in terms of dosage and clinical subgroups (neurotic, involutional, manic-depressive). The best therapeutic response occurred with 50mg/day dosage in the depressive neurosis and involutional melancholia groups, while comparable results were obtained in manic-depressive illness with 150mg/day dosage. As for plasma drug concentrations, the neurotic patients showed a more favorable response in the presence of lower amitriptyline and nortriptyline plasma levels. No significant differences were observed between mean plasma concentration of the responders and nonresponders. It is concluded that in some cases, plasma monitoring might prove helpful in clinical practice. 18 references. (Author abstract modified)

004676 Daiguji, Makoto; Meltzer, Herbert Y.; U'Prichard, David C. Dept. of Pharmacology, Northwestern Univesity School of Medicine, Chicago, IL 60611 **Human platelet alpha2-adrenergic receptors: labeling with 3H-yohimbine, a selective antagonist ligand.** Life Sciences. 28(24):2705-2717, 1981.

The high affinity labeling of human platelet alpha2-adrenergic receptors with 3H-yohimbine is reported, and the utility of 3H-yohimbine as an antagonist probe of platelet alpha2-adrenergic receptors is discussed. Binding was rapid and reversible at 25 degrees C. Both saturation and kinetic experiments indicated a single order of binding sites. The 3H-yohimbine site exhibited alpha2-receptor specificity: (-)-norepinephrine and (-)-isoproterenol were 4.8 and 330 times less potent than (-)-epinephrine; (-)-catecholamines were 17 to 35 times more potent than corresponding ()-catecholamines; the selective alphal-antagonist prazosin was 340 times less potent than yohimbine. Catecholamine agonists exhibited shallow curves in inhibiting 3H-yohimbine binding. 3H-yohimbine labeled fewer platelet sites than did 3H-dihydroergocryptine under identical conidtions, and may be a more specific and useful antagonist probe of platelet alpha2-receptors than 3H-dihydroergocryptine. 45 references. (Author abstract modified)

004677 Elton, R. A.; Tiplady, B. Medical Statistics and Computing Unit, University of Edinburgh, Edinburgh, Scotland **Mild, moderate, severe – the statistical analysis of short ordinal scales.** Neuropharmacology. 19(12):1239, 1980.

A modification of the (1946) Wilcoxon stratified sum of ranks test, which is designed for use with short ordinal scales such as those used for collecting side-effects, or the individual items from the Hamilton Rating Scale for depression, stratifying the data according to the initial (pretreatment) score on the scale, is presented. The test has two important advantages over an unstratified test: 1) it permits meaningful analysis of data where baseline levels differ markedly; and 2) it allows for the correlation of pretreatment and postreatment scores, which may lead to increase in power. 1 reference.

004678 Ghose, K. Lingfield Hospital School, St. Piers Lane, Lingfield, Surrey RH7 6PN, England **Sympathomimetic amines and tricyclic antidepressant drugs.** Neuropharmacology. 19(12):1251-1254, 1980.

The pharmacological effects of various sympathomimetic amines and tricyclic antidepressant drugs were studied by three different methods: pressor response test; pupil diameter; and hand vein diameter. The pressor response test was observed to be the most reliable reproducible, and relatively safe technique. Decreased tyramine sensitivity not only correlated with the plasma drug concentrations but also with other pharmacodynamic measurements. Measurements of pupil diameter and dorsal hand vein diameter to assess the mydriatic and venoconstrictor effects of drugs should be considered in patients with cardiovascular disorders where systemic pressor amines are contraindicated. 14 references.

004679 Hanin, Israel; Koslow, Stephen H. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Physico-chemical methodologies in psychiatric research.** New York, Raven Press, 1980. 265 p. $26.50.

New physicochemical methodologies in neuropsychiatric research are reviewed, including high performance liquid chromatography, radioimmunoassay, radioreceptor assays, gas chromatography/mass spectrometry, chromosome banding, and fibroblast cultures. The basic principles of each technique are outlined, and the advantages and disadvantages of the new techniques are considered in relation to alternative methods. Applications of each technique to problems in neuropsychiatry are described.

004680 Itil, Turan M. Center for Biological Psychiatry, V.A. Health Care Facility, Montrose, NY 10548 **Computer-analyzed eletroencephalogram to predict the therapeutic outcome in schizophrenia.** In: Baxter, C., Perspectives in schizophrenia research. New York, Raven Press, 1980. 445 p. (p. 61-80).

Specialized EEG investigations with child and adult schizophrenics, high-risk children, and antipsychotic (neuroleptic) drugs suggest that computer analyzed EEGs (CEEGs) can be used to predict the therapeutic outcome in schizophrenia, particularly when the modality is treatment by pharmaceuticals. Based on the test dose procedures which use CEEGs, it may be possible to tailor the type of the drug treatment and the dosage for each individual patient. A typical CEEG response of a schizophrenic patient to a neuroleptic compound indicates that this drug is adequately absorbed, properly metabolized, penetrated through the blood-brain barrier, and has noticeable effects on the brain function of the patient. The patients known to be resistent to neuroleptic drug treatments (therapy-refractory schizophrenics) do not show a typical neuroleptic response to a test dose neuroleptic. In contrast they show a response which is similar to that seen after psychostimulant administration in normal subjects. A discussion of the paper follows. 41 references. (Author abstract modified)

004681 Jatlow, Peter. Dept. of Laboratory Medicine, Yale-New Haven Hospital, 789 Howard Avenue, New Haven, CT 06504 **Therapeutic monitoring of plasma concentrations of tricyclic antidepressants: perspective of the clinical laboratory.** Archives of Pathology and Laboratory Medicine. 104:341-344, 1980.

Therapeutic monitoring of plasma concentrations of tricyclic antidepressants (TCAs) is reviewed in relation to the functioning of the clinical laboratory. It is noted that therapeutic ranges for plasma concentrations of the TCAs have not been established with the same degree of certainty as for other commonly monitored drugs, such as antiepileptic and cardioactive agents. Nevertheless, sufficient information is presently available to suggest that measurement of TCAs in appropriate circumstances can be helpful in managing the pharmacotherapy of depressed patients. Presently available techniques for measuring TCAs are time consuming and costly. Clinical research relevant to understanding the significance of plasma levels, as well as their actual clinical application, would benefit from the development of a reliable, relatively convenient, and inexpensive assay. 41 references. (Author abstract modified)

004682 Javaid, Javaid I.; Pandey, Ghanshyam N.; Duslak, Barbara; Hu, Hsiang-Yun; Davis, John M. Illinois State Psychiatric

Institute, Dept. of Research, 1601 West Taylor Street, Chicago, IL 60612 **Measurement of neuroleptic concentrations by GLC and radioreceptor assay.** Communications in Psychopharmacology. 4(6):467-475, 1980.

Drug concentrations in plasma from patients treated with different neuroleptics were measured by fluorometric and gas liquid chromatographic (GLC) methods and compared with neuroleptic activity as measured by radioreceptor assay (RRA). After treatment with therapeutic doses of thioridazine the results obtained by spectrofluorometric assay and RRA correlated highly (r=.95, p less than .001). The butaperazine levels measured by GLC correlated significantly with RRA values (p less than .05), although the correlation was only fair (r=.64). The similar values obtained by two methods (RRA/GLC ratio=1.3) would suggest that butaperazine probably does not have many active metabolites. Similarly, there was a significant correlation (r=.62, p less than .01) for haloperidol levels in plasma, and the RRA/GLC ratio was 1.4. On the other hand, neuroleptic activity in plasma after treatment with fluphenazine and trifluoperazine was seven to eight times greater than the drug levels measured by GLC. The correlation between the two methods for fluphenazine was highly significant (r=.85, p less than .001) although there was no correlation for trifluoperazine. These results suggest that simultaneous use of GLC and RRA may be useful in studies of neuroleptics and their pharmacologically active metabolites. 14 references. (Author abstract)

004683 Jenden, Donald J. School of Medicine, University of California, Los Angeles, CA GC-MS/**stable isotopic analyses for deanol, choline, and their acetyl esters.** In: Klein, E., Stable isotopes. New York, Academic Press, 1979. (p. 403-410).

Rigorous GC-MS methods were developed for the analysis of deanol (N,N-dimethylaminoethanol) and choline in the same sample. Two basic approaches were used. The first employs extraction of deanol into chloroform from an aqueous solution adjusted to pH 11 with lithium hydroxide and saturated with lithium citrate to maximize the partition coefficient. The aqueous solution is then extracted with dipicrylamine to remove the choline and both fractions are analyzed. The second approach, best used in experimental studies, uses bis-(methyl-2H2)-deanol in place of labeled compound and analyzed with the same internal standards. Choline, deanol, and their O-acetates are quantitatively extracted into dichloromethane with dipicrylamine and may be simultaneously measured. These measurements remain compatible with the use of (ethylene-2H4)-choline as a kinetic tracer to measure rates of choline uptake and acetylation. These methods were used in a reinvestigation of the metabolism and effects of deanol on cholinergic mechanisms in rat brain, both in vivo and in vitro, and on choline uptake and acetylation in guinea-pig myenteric plexus. 40 references. (Author abstract modified)

004684 Kawashima, Koichiro; Ishijima, Buichi; Yoshimizu, Nobuhiro; Sato, Fumiaki. Dept. of Pharmacology, Jichi Medical School, Minamikawachi-machi, Tochigi-ken 329-04, Japan **A comparison of radioimmunoassay with spectrophotometry for the determination of plasma diphenylhydantoin concentrations.** Japanese Journal of Pharmacology. 30(5):752-755, 1980.

The precision and accuracy of a new radioimmunoassay (RIA) for diphenylhydantoin (DPH) were evaluated. In samples obtained from 51 epileptic patients on DPH and phenobarbital for more than 1 month, DPH values determined by the RIA were significantly correlated with values obtained by spectrophotometry. DPH can be determined from a small volume of plasma without extraction for the RIA. 11 references.

004685 Koslow, Stephen H. Biologic Research Section, NIMH, Rockville, MD 20857 **A quantitative probe for biological psychiatry: selected ion monitoring.** In: Hanin, I., Physico-chemical methodologies in psychiatric research. New York, Raven Press, 1980. 265 p. (p. 155-170).

The use of selected in monitoring which combines the resolving power of gas chromatography (GC) with the sensitivity and specificity of mass spectrometry (MS), to measure endogenous and exogenous substances in animals and man is reviewed. With GC/MS, it is possible to measure levels of neurotransmitters and their metabolites in human cerebrospinal fluid and in discrete brain nuclei of animals. In psychiatry, GC/MS is used to measure plasma levels of drugs and their metabolites to determine when therapeutic levels have been attained. Future use of GC/MS with stable isotopes and with laser microprobes will facilitate studies of molecular mechanisms in situ and in vivo. Acceptance of GC/MS technology by the clinical sciences will aid in diagnosis, definition of disorders and their etiological mechanisms, and plasma drug level monitoring in pharmacotherapy. 56 references.

004686 Kragh-Sorensen, Per. no address **The use of clinical kinetic data in treatment with antidepressant drugs.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):157-167, 1980.

The use of clinical kinetic data in treatment with antidepressant drugs is discussed. It is claimed that determination of plasma levels of tricyclic antidepressants in contemporary clinical psychiatry is of value only for two drugs, nortriptyline (NT) and imipramine (IP). The therapeutic plasma concentration range defined for these two drugs is valid only for patients suffering from endogenous depression, and this type of depression represents only a minority of patients treated with tricyclic antidepressants. However, in this group of patients, the therapeutic effect of tricyclic antidepressants is usually most clearly drug related. The need for a better system for classification of depressive disorders is emphasized. A panel discussion of these topics is appended. 27 references.

004687 Mathis, Donald F.; Budd, Robert D. Rancho Los Amigos Hospital, Downey, CA 90242 **GLC/TLC analysis of codeine and morphine in urine via derivatization techniques.** Clinical Toxicology. 16(2):181-188, 1980.

A procedure for thin layer chromatographic (TLC) and gas/liquid chromatographic analysis of codeine and morphine derivatives in urine is described. The procedure can be used in cases where there is too much interference for TLC analysis as free drugs. Codeine and morphine can be detected without interference at concentrations as low as 0.3mcg/mL. 5 references. (Author abstract modified)

004688 Moss, W. W.; Posey, F. T.; Peterson, P. C. no address **A multivariate analysis of the infrared spectra of drugs of abuse.** Journal of Forensic Sciences. 25:304-313, 1980.

The infrared (IR) spectra of 15 drugs of abuse were analyzed for similarity by using techniques of numerical taxonomy. The study included six barbiturates (amorbarbital, barbital, butabarbital, phentobarbital, phenobarbital, and secobarbital), four amphetamine related compounds (amphetamine, ephedrine, metamphetamine, and phentermine), and five other drugs (cocaine, heroin, phencyclidine, phendimetrazine, and diazepam). Three character sets were based on increasing numbers (10, 24, and 36) of IR peaks. The cluster analysis, principal component analysis, and nonmetric multidimensional scaling elements of the program system NT-SYS were used to structure taxonomic distances between drugs. Best results were obtained from the 36 peak data set; ordination diagrams proved to be more visually informative than phenograms. Preliminary results from analysis of this set of drugs indicate that an expanded multivariate approach to drug classification may be useful. (Journal abstract)

004689 Paul, S. M.; Rehavi, M.; Hulihan, B.; Skolnick, P.; Goodwin, F. K. Clinical Psychobiology Branch, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20205 **A rapid and sensitive radioreceptor assay for tertiary amine tricyclic antidepressants.** Communications in Psychopharmacology. 4(6):487-494, 1980.

A rapid and sensitive radioreceptor assay for tertiary amine tricyclic antidepressants is described. As psychotropic drugs, including the tricyclic antidepressants, are among the most commonly prescribed agents, and as careful monitoring of the plasma concentration of the parent drug and its pharmacologically active metabolites can be useful in monitoring compliance and in adjusting doses for therapeutic purposes, this method can prove useful in clinical management. The method has been applied to clinical samples from patients taking imipramine with good results. At present, the method is only capable of quantitating the parent tertiary amine tricyclic antidepressants. 6 references. (Author abstract modified)

004690 Pearce, Dan; Wiersema, Sandra; Kuo, Margaret; Emery, Carole. Forensic Science Services, Office of the Sheriff-Coroner, Santa Ana, CA 92702 **Simultaneous determination of morphine and codeine in blood by use of select ion monitoring and deuterated internal standards.** Clinical Toxicology. 14(2):161-168, 1979.

A select ion monitoring procedure for the simultaneous determination of morphine and codeine in blood is described. A gas chromatograph/mass spectrometer is coupled with a data system, and deuterated morphine and codeine are used as internal standards. Inclusion of morphine and codeine in a single analysis decreases sample preparation and analysis time. 14 references.

004691 Pittman, Kenneth A.; Smyth, Robert D.; Mayol, Robert F. Bristol Laboratories, Syracuse, NY 13201 **Serum levels of butorphanol by radioimmunoassay.** Journal of Pharmaceutical Sciences. 69(2):160-163, 1980.

A radioimmunoassay was developed for the analysis of butorphanol in human serum. The procedure involves extraction of serum with hexane containing 2% isoamyl alcohol, followed by evaporative solvent removal and radioimmunoassay of the reconstituted residue. The antibody significantly cross-reacts with unidentified butorphanol metabolites but not with the known metabolities, hydroxybutorphanol and norbutorphanol. Extraction eliminated interference from butorphanol metabolities normally present in serum. The antibody also cross-reacts with pentazocine and cyclazocine, but not with morphine, hydromorphine, oxymorphine, codeine, methadone, or meperidine. After i.v. administration of 2mg butorphanol tartrate to male volunteers, serum butorphanol levels declined biexponentially with an average terminal half-life of 2.7 hours. 18 references. (Author abstract modified)

004692 Reed, Dwight. Forensic Science Services, 550 N. Flower St., Room 201, P.O. Box 449, Santa Ana, CA 92702 **Comparison of spectrofluorometric and GC/MS procedures for the quantitation of morphine in blood and brain.** Clinical Toxicology. 14(2):169-180, 1979.

Morphine levels in blood and brain were determined postmortem by spectrofluorometry and by gas chromatography/mass spectrometry (GC/MS). In both blood and brain, morphine values obtained by spectrofluorometry were about one half those obtained by GC/MS. In 7 of 38 blood samples, morphine was detected by GC/MS but not by spectrofluorometry. In 2 of 55 blood samples analyzed before and after hydrolysis, morphine was detectable only after hydrolysis. 14 references.

004693 Robinson, Katherine; Rutterford, Mary G.; Smith, R. N. Smith: Metropolitan Police Forensic Science Laboratory, 109 Lambeth Road, London SE1 7LP, England **A sensitive benzodiazepine radioimmunoassay of broad specificity.** Journal of Pharmacy and Pharmacology. 32(11):773-777, 1980.

A benzodiazepine radioimmunoassay that can detect subtherapeutic levels of bromazepam, chlordiazepoxide, clobazam, demoxepam, desalkylflurazepam, desmethyldiazepam, diazepam, flunitrazepam, lorazepam, medazepam, nitrazepam, oxazepam, prazepam, temazepam, and triazolam, is described. The standard curve for diazepam has a concentration range of 0 to 2.5mg/ml. The assay requires a 75mcl sample and is particularly applicable to blood samples of forensic interest that may be hemolysed or decomposing. 27 references. (Author abstract modified)

004694 Smith, Robert C.; Vroulis, George; Misra, Chandra H.; Schoolar, Joseph; DeJohn, Charles; Korivi, Prabhavathy; Leelavathi, D. E.; Arzu, Dorita. Section of Biological Psychiatry, Texas Research Institute of Mental Sciences, 1300 Moursund, Houston, TX 77030 **Receptor techniques in the study of plasma levels of neuroleptics and antidepressant drugs.** Communications in Psychopharmacology. 4(6):451-465, 1980.

The relationship of gas liquid chromotography (GLC) to radioreceptor (RR) assay of neuroleptics and antidepressants was assessed in schizophrenic and depressed patients. There was a moderate but statistically significant relationship between GLC and RR assays of haloperidol, but no relationship between RR and GLC assays of nortriptyline. Preliminary analysis suggests that RR assays of haloperidol did not correlate with clinical response. RR assays of neuroleptics did significantly correlate with some side-effects of these medications. There was a significant positive correlation of RR plasma levels and subjective side-effects of haloperidol, and a significant negative correlation with tardive dyskinesia scores. RR assays of nortriptyline correlated significantly with cardiovascular side-effects of the medication in depressed patients. 11 references. (Author abstract)

004695 Vitaliano, Peter Paul; Prinz, Patricia; Vitiello, Michael V.; Olshan, Andrew; Roehrs, Timothy A. Dept. of Psychiatry and Behavioral Sciences, RP-10, University of Washington, Seattle, WA 98195 **On the use of repeated measures designs in psychopharmacology.** Psychopharmacology. 72(3):247-249, 1981.

The use of the repeated measures design in psychopharmacology is discussed. Since the test of equal means across repeated trials requires an assumption of compound symmetry that is often untenable, it can lead to erroneous interpretations. Three approaches that can minimize this bias are described based on data from a study of the effects of alcohol on growth hormone levels. 10 references. (Author abstract modified)

004696 Woggon, B.; Dittrich, A.; von Luckner, N.; Keller, W. Psychiatrische Universitatsklinik Zurich, Forschungsdirektion, Postfach 68, CH-8029 Zurich, Switzerland **/Study on the stability of the factorial structure of the AMP system during treatment./** Untersuchung zur Stabilitat der faktoriellen Struktur des AMP-Systems im Behandlungsverlauf. International Pharmacopsychiatry. 15(6):350-364, 1980.

The stability of the factorial structure of the AMP system was studied on days 0, 5, 10, and 20 of psychopharmacological treatments of 396 patients mainly suffering from endogenous psychoses. The analysis was based on a reduced item pool of 52 items, which occurred on day 20 in at least 10% of patients. For the nine factor solution the factorial structure was stable during treatment for the apathic, the hallucinatory-disintegrative, and the retarded-depressive syndromes as well as for the hostility syndrome. The other five AMP syndromes showed no stable structure during the treatment. On the other hand, the factorial structure of the two factor solution was found to be stable on days 0, 5, 10, and 20 without exception. These results should be considered when using the AMP system for the documentation of syndromes during the course of therapeutic trials. 21 references. (Author abstract)

17 MISCELLANEOUS

004697 Adler, Martin W. Dept. of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **Mini-Symposium. I. The in vivo differentiation of opiate receptors: introduction.** Life Sciences. 28(14):1543-1545, 1981.

Trends in the research literature concerning in vivo differentiation of opiate receptors are outlined. It is noted that there now seems to be general acceptance of opiate receptor heterogeneity, although absolute proof is still lacking. Just as specific pharmacological antagonists were necessary to prove mulitple receptors in other systems, so are they necessary here. Representative examples of in vivo studies that have postulated multiple opiate receptors using a variety of tests and species are cited. The need for universally understood system of nomenclature for the opiate receptors is emphasized. 20 references.

004698 Albert, E. Psychiatrisches Landeskrankenhaus Eichberg, Eltville/Rhein, West Germany **/Senile dementia in its still guidable initial phase./** Die senile Demenz in ihrem noch lenkbaren Initialstadium. Neurologie und Psychiatrie fur die Praxis. 5:396-401, 1979.

Aspects for the treatment of senile dementia, which seems to be in its final phase and is merging into Alzheimer illness, are discussed. Acute, cardiac conditioned symptoms can often be observed at the beginning of senile dementia, and can be treated with Strophantin. Examples are given from cases which should not but do occur in modern nursing facilities. A particular clinical situation is reported exhibiting illogical thoughtforms, an expression which has been used in connection with schizophrenia. (Journal abstract modified)

004699 Avrutskiy, G. Ya. Otdel terapii i reabilitatsii, Moskovskiy institut psikhiatrii, Ministerstvo zdravookhraneniya RSFSR, Moskva, USSR **/Changes in the clinical picture and the course of psychoses during massive psychopharmacotherapy and the significance of these changes for improvements in psychiatric treatment./** Izmeneniya kliniki i techeniya psikhozov v itoge massovoy psikhofarmakoterapii i ikh znacheniye dlya sovershenstvovaniya lechebnoy pomoshchi. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 79(9):1387-1394, 1979.

Changes in the clinical picture and course of psychoses during massive psychopharmacotherapy are discussed in relation to the effects of these changes on improvement in psychiatric treatment. Significant changes in the clinical picture and course of psychoses, the predominance of reduced (outpatient) forms of psychoses, the therapeutic lability of psychopathological symptoms, and the necessity for a combination of medicinal and sociorehabilitational therapy have made it possible to change the emphasis from inpatient to outpatient treatment. It is concluded that outpatient therapy is desirable both because it is economical and because it makes possible the maximum use of the advantages of medicinal therapy, thereby making it possible to treat patients without removing them from their usual social and work environment. This sharply increases the effectiveness of the treatment. 35 references.

004700 Axelsson, R.; Ohman, R. no address **On monoaminergic interaction with behaviour-modifying peptide hormones.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):219-229, 1980.

The interaction between nervous and hormonal mechanisms at the hypothalamic and pituitary level is reviewed in relation to the neuroanatomical and biochemical characteristics of this region. A model is proposed for the dopamine regulation of prolactin, in which interindividual differences in sensitivity to neuroleptic drugs can be assessed. A possible method for prediction of optimal dosage of neuroleptic drugs is described together with a clinical study in which the prolactin response to treatment of psychotic patients with thioridazine is related to antipsychotic effect. A panel discussion of these topics is appended. 22 references.

004701 Ban, Thomas A. Psychiatry Dept., Vanderbilt University, Nashville, TN 37203 **Psychopharmacology for the aged.** Basel, Switzerland, S. Karger, 1980. 216 p. $23.50.

Recent research findings relevant to the clinical management of elderly patients manifesting mental or emotional disorders are reviewed in detail. Epidemiology, behavioral aspects, and possible prevention of aging are discussed. The psychopathology found in the elderly is outlined, as well as the pharmacology of all drugs commonly used in the treatment of these conditions. Pharmacokinetics, adverse effects, and drug interactions are described. A number of drugs being used to influence either cerebral blood flow or brain metabolism in the common chronic brain syndromes are discussed. Controversial questions about the use of drugs with euphoric properties in the treatment of demented and dying patients are considered. Over 1,400 references are included.

004702 Ban, Thomas A.; Wilson, William H.; McEvoy, Joseph P. Dept. of Psychiatry, Vanderbilt University, 1501 Murfreesboro Road, Nashville, TN 37217 **Amoxapine: a review of literature.** International Pharmacopsychiatry. 15(3):166-170, 1980.

The literature is reviewed on the new antidepressant amoxapine, a tricyclic dibenzoxazepine compound, the demethylated metabolite of the neuroleptic loxapine. In animal pharmacological studies, amoxapine has shown striking similarities to imipramine. In contrast to the prototype antidepressant drug, however, amoxapine does not interact with serotonin. In 10 uncontrolled clinical trials, amoxapine was shown to have antidepressant effects in the dosage range of 100 to 300mg/day. This was verified in 10 published standard, and placebo and standard controlled clinical studies in which amoxapine was superior to placebo and equal in overall therapeutic efficacy to imipramine and amitriptyline. Side-effects were similar to those of the reference drugs. 21 references. (Author abstract modified)

004703 Berger, Philip A.; Davis, Kenneth L.; Hollister, Leo E. Veterans Adminstration Hospital, Palo Alto, CA 94304 **Cholinomimetics in mania, schizophrenia, and memory disorders.** In: Barbeau, A., Nutrition and the brain. New York, Raven, 1979. v.5. (p. 425-441).

The use of cholinomimetics in manic psychosis, schizophrenia, and senile dementia is reviewed. Evidence is presented that short acting cholinomimetics, particularly the acetylcholinesterase inhibitor physostigmine, produce a transient reversal of the symptoms of mania. In addition, both short and longer acting cholinomimetics are sometimes reported to cause depression in Ss without mania. Taken together, these findings suggest that a relatively nontoxic, long acting, cholinomimetic-like choline or lecithin should be given a trial in patients with mania. Although neuroleptics were found to be superior to choline chloride in the treatment of schizophrenia, choline chloride was associated with modest improvement of some symptoms in most patients. Since manic patients may also respond to cholinomimetics, patients with schizoaffective schizophrenia, manic type, may be the best Ss for further trials of long acting cholinergic agents. Human studies with anticholinergics and cholinomimetics suggest that the long-term memory process of storage, and perhaps retrieval, can be improved by cholinomimetics. However, administration of variable dosages of choline chloride to Alzheimer's patients and normal elderly Ss with minor memory impairment have yielded inconclusive results. 105 references.

004704 Buckalew, L. W.; Ross, Sherman; Starr, B. James. Dept. of Psychology, Alabama A&M University, Normal, AL 35762 **Nonspecific factors in drug effects: placebo personality.** Psychological Reports. 48(1):3-8, 1981.

Evidence relating to personality correlates of responsivity to placebos is reviewed. It is concluded that a trait model of responsivity is largely unsubstantiated, and that other nonspecific factors of drug effects may be more influential in reactions to placebos. Evaluation of measures of response to placebos and methodological issues is needed. Potential neurochemical substrates for the action of placebos are suggested as being promising. 44 references. (Author abstract modified)

004705 Bunney, W. E., Jr.; Tallman, J. F. Section on Psychiatry, Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **New biological research relevant to anxiety.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(5):273-276, 1980.

Through a review of new biological research with both animals and man of the physiology and mode of action of the most effective anxiolytic drugs (the benzodiazepines (BDZs)), a better understanding of anxiety is attempted. The following areas are discussed: the discovery of brain receptors for BDZs (these binding sites may mediate the pharmacological activity of the BDZs, the action of BDZ, the possible enhancement by BDZ of the inhibitory neurotransmitter GABA, the search for endogenous BDZ in the brain, the criteria for defining a BDZ receptor in the brain, and the possible role of the locus coeruleus in anxiety. Chlordiazepoxide and diazepam are the most widely used BDZs for treating anxiety. Four distinct behavioral properties of BDZ in man include: anticonvulsant, muscle relaxant, sedative/hypnotic, and anxiolytic (which may result from a combination of the former three properties). Evidence is provided that BDZ may produce alterations in the postsynaptic response to GABA, that BDZ modulates GABA mediated synapse events and potentiates GABAergic inhibition in the central nervous system. Potential applications of the discovery of a binding site for BDZ in the brain and research concerning piperoxane, an alpha-adrenergic blocker which increases anxiety, are discussed. 25 references.

004706 Bush, Patricia J. no address **Drugs, alcohol and sex.** New York, Richard Marek, 1980. 287 p. $12.95.

The influences of drugs and alcohol on sexual desire, performance, activity, and experience are described. The possibilities of affecting sex life through the use of aphrodisiacs, prescribed and over the counter medicines, oral contraceptives, and recreational drugs (alcohol, marihuana, cocaine, amphetamine, volatile inhalants, barbiturates, heroin, and psychedelics) are discussed. Drug effects on libido, on potency, on orgasm, on ejaculation, and on the reproductive system are presented in an appendix.

004707 Coppen, A.; Al-Yassiri, M. M.; Briley, M. S.; Burgess, C. E.; Clements-Jewery, S.; Davies, B.; Leonard, B. E.; Montgomery, S. no address **Do we need any more antidepressants?** Neuropharmacology. 19(12):1201-1206, 1980.

A roundtable discussion on the need for more antidepressants is presented. Topics discussed include: the need for more precise knowledge of the pathophysiology of depressive disorders; the relative efficacy of the first and second generation antidepressants; bridging the gap between animal studies and the clinical use of antidepressant drugs; the importance of side-effects for compliance; cross-cultural aspects of psychopharmacology; changes in receptor sensitivity; and prescription patterns of various antidepressants.

004708 Cowdry, Rex W.; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Building 10, Room 4S239, Bethesda, MD 20014 **Biological and physiological predictors of drug response. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 65 p.

Research on biological drug response predictors in the major psychiatric syndromes is reviewed in the hope of establishing a more rational and integrated approach to pharmacologic treatment of mental disorders. A conceptual model for exploring interrelationships in psychobiology is described which emphasizes the three main spheres of information about an individual patient: clinical variables, biological findings, and pharmacologic response. An underlying biological current involving monoamine neurotransmitter mechanisms is identified in much of the research, and a pathogenetic model for psychiatric syndromes based on the amine hypothesis is described, along with the effects of pharmacologic agents on monoamine systems. Two types of biological predictors are identified (pretreatment factors and those that are made during treatment), and these are used to examine the following psychiatric conditions: 1) depression (including its endogenous/endogenomorphic occurrence), the unipolar/bipolar distinction, a typical depression and delusional depressions and its treatment with tricyclic antidepressants; 2) functional psychoses, especially schizophrenia and mania; 3) alcoholism; 4) aggressive behavior; and 5) hyperkinesis. 159 references.

004709 Cuche, H.; Deniker, P. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Hopital St. Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France **Psychiatric uses of beta-blockers.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(5):267-272, 1980.

A review is presented of the psychiatric applications of beta-blockers, such as propanolol, pindolol, oxprenolol, and acebutolol. The main clinical trials and the principal side-effects of beta-blockers are discussed, and alpha agents and receptors and beta receptors and agents, which interact with the noradrenergic system, are considered. Psychopharmacological trials with beta-blockers are reported for treating patients with the following disorders: acute variegate porphyria, postpartum psychosis, severe psychosis (those experiencing excitation, manic depression, anxiety, hallucinations, withdrawal with tension, and affective disorders), schizophrenia, paranoid patients with a chronic delusional state, and alcoholism. Methodological problems are considered and longer double-blind clinical trials are recommended. The side-effects reported with beta-blockers are: neurological side-effects, sleep disorders, toxic symptoms, cardiovascular symptoms, depressive complications, and gastrointestinal problems. No long-term toxic effects of beta-blockers have been reported, and the administration of two doses/day with a slow increase of the daily dosage is believed to constitute a safe treatment method. The guides for monitoring beta-blockers in psychiatric therapy are pulse, blood pressure, and the patient's mental state. It is concluded that beta-blockers are the accepted treatment for anxiety with somatic symptoms. 34 references.

004710 Eisdorfer, Carl; Fann, William E. Dept. of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, Seattle, WA 98105 **Psychopharmacology of aging.** New York, SP Medical and Scientific Books, 1980. 271 p.

Research on the interaction between aging and psychoactive medication and its effect on adaptation is reviewed in support of the view that an understanding of drug use consequences, misuse, and abuse of drugs among the elderly is a salient issue for the scientist, clinical physician, and other health care professionals. Topics include: 1) sleep changes that occur with aging; 2) enzymatic changes in the aging brain and aspects of its pharmacological intervention with ergot compounds; 3) assessment of age related changes in learning and performance in the rat; 4) pathophysiology and experimental pharmacology in gerontological brain research; 5) the use of tricyclic antidepressant drugs in geriatric patients; 6) comparative stereology of capillaries in the cerebral cortex, with specific reference to drug effects; 7) qualitative studies in the cerebral cortex of elderly persons; 8) aging and the behavioral effects of dopamine agonists in rodents; 9) neurochemical changes in the aging human and nonhuman primate brain; 10) pharmacokinetics in geriatric psychopharmacology; and 11) the cyclic nucleotide system in the brain during development and aging.

004711 Fichter, M. M.; Wuschner-Stockheim, M. MPI Psychiatrie, Munchen, West Germany /**Anorexia nervosa. Symptoms, course and possibilities for treatment.**/ Die Pubertatsmagersucht. Symptomatik, Verlauf und Behandlungsmoglichkeiten. Padiatrische Praxis. 22:411-422, 1979.

Anorexia nervosa is discussed as a nosological unit, not as a special form of schizophrenia or depression. The symptomatology of anorexia nervosa is described in six groups of disturbances, with reference to psychological, social cultural, and physical factors. Prognostic moments such as the age of onset of illness, other neurotic symptoms, duration of illness, and expected course are analyzed. It is concluded that somatic methods such as electroshock, hormone treatment, anabolica, neuroleptic treatment, and prefrontal lobotomy, as well as psychoanalysis and behavioral therapy, are effective in treating anorexia nervosa patients. (Journal abstract modified)

004712 Freedman, A. M. Dept. of Psychiatry, New York Medical College, Valhalla, NY **Psychopharmacology and psychotherapy in the treatment of anxiety.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(5):277-289, 1980.

Psychopharmacology and psychotherapy, the two modalities for the treatment of anxiety, are evaluated, and associated literature is reviewed. Difficulties are discussed with regard to defining and recognizing anxiety, which is a manifestation encountered in a heterogeneous group of syndromes or disorders that presents itself psychologically, somatically, and behaviorally. The following recommendations and conclusions are made: the development of the best treatment or combination of treatments appropriate for each specific case or group of cases is essential; controlled comparative studies indicate that patients receiving psychotherapy for anxiety symptoms do better than do controlled groups; no one method of psychotherapy has been found to be superior; pharmacotherapy alone in treating anxiety has been proven effective; combined therapy of pharmacological agents and psychotherapy appears to be superior to either modality alone; and critical research and expanded knowledge of both the existing modalities of treatment and the neurological considerations of anxiety are warranted. 50 references.

004713 Gadow, Kenneth D. State University of New York, Stony Brook, NY 11790 **Prevalence of drug treatment for hyperactivity and other childhood behavior disorders.** In: Gadow, K., Psychosocial aspects of drug treatment for hyperactivity. Boulder, CO, Westview, 1979. 479 p. (p. 13-76).

The results of drug prevalence studies in the treatment of hyperactivity and other childhood behavior disorders from six different geographic locations are discussed. The findings pertain to public and parochial schools and to special education classrooms, and are seen as important due to allegations that psychotropic drugs are prescribed indiscriminantly to large numbers of such children. Patterns of drug treatment (preferred drugs, dosage and schedule, polypharmacy, age at start of medication, and duration of treatment) are treated, along with psychosocial aspects of drug prevalence (interaction of rate and SES), national estimates of the extent of drug use, nondrug therapies, and methodological issues. 104 references. (Author abstract modified)

004714 Gadow, Kenneth D.; Loney, Jan. State University of New York, Stony Brook, NY 11790 **Psychosocial aspects of drug treatment for hyperactivity.** AAAS Selected Symposia Series. Boulder, CO, Westview, 1979. 479 p.

The pattern of drug and nondrug treatments for hyperactivity, as well as methodological problems encountered in evaluating treatment outcomes, is examined. Diagnostic, treatment, and outcome issues in hyperkinesis are emphasized. Specific topics include: the measurement of hyperactive behavior in children and adolescents; the effects of methylphenidate (Ritalin) as a stimulant drug, on symptoms; the degree of school, family, and medical involvement in drug therapy; and the status of hyperactive children as young adults.

004715 Gal, E. M. Dept. of Psychiatry, University of Iowa College of Medicine, Iowa City, IA 52240 **Cerebral fluoride in mania and the effect of lithium: a hypothesis.** Communications in Psychopharmacology. 4(5):405-409, 1980.

The hypothesis that the ratio between ionic and bound fluoride is genetically altered in certain target areas of the brain during manic episodes is discussed. According to this hypothesis, a shift in favor of the ionic fluoride results in increased cyclic AMP, intracellular Na, and prostaglandin E1 synthesis. The action of lithium in mania could be due to the conversion of the hydrophilic fluoride ion into the hydrophobic LiF or into a double lithium/fluoride/protein complex, thus releasing the inhibitory effects of ionic fluoride at active sites like membrane adenosine triphosphatase or adenyl cyclase. Empirical tests of this hypothesis are suggested. 15 references. (Author abstract modified)

004716 Gee, Susan. Reports and Statistics Service, Veterans Administration, Washington, DC **Psychiatric drug study. Part II. Mental Hygiene Clinic Survey, Day Treatment Center Survey, Day Hospital Survey.** Springfield, VA, NTIS, PB82-142563, 1980. 134 p.

The use of psychiatric drugs in three Veterans Administration (VA) outpatient treatment settings (mental hygiene clinics, day treatment centers, and day hospitals) is described in the second of three reports on the 1978 Psychiatric Drug Survey. No attempt is made to evaluate the ordering practices or the effectiveness of treatment. Correlation between diagnoses and drug orders is evaluated, and data on the distribution of antipsychotic, anxiolytic, antidepressant, antiparkinson, sedative hypnotic, and other drugs are analyzed. Additionally, the incidence of tardive dyskinesia and the types of drugs causing the syndrome are described. (Journal abstract modified)

004717 Guandalini, Andrea; Interlandi, Gaetano; Bricolo, Renato; Odorizzi, Franco; Frazingaro, Silvio. Ospedali Neuropsichiatrici Provinciali di Verona-Marzana, Verona-Marzana, Italy /**Psychotropic drugs and psychiatric hospital admissions in Verona, Italy.**/ Psicofarmaci e assistenza psichiatrica nel veronese. Lavoro Neuropsichiatrico. 66(3):103-115, 1980.

The effects of Law 180, which mandates deinstitutionalization and reorganization of Italy's hospitals for the mentally ill, are summarized in terms of patient admissions and drug use. Tables show the decline of both patient admissions and drug use over the period 1965 to 1977. The decrease in use of psychotropic drugs is deemed attributable to a more rational and selective policy, with resultant decrease in cost. In contrast, the cost of government subsidies and social assistance programs is on the rise. 8 references. (Journal abstract modified)

004718 Harrer, G. Landesnervenklinik, Salzburg, Austria / **Therapeutic treatment of insufficient performance in cerebrovascular diseases.**/ Zur Therapie der Leistungsinsuffizienz bei zerebrovaskularen Erkrankungen. Medizinische Welt. 30:1320-1323, 1979.

Therapy and rehabilitative effectiveness to remove paresis, coordinating disturbances, and brain pathological blackouts in cerebrovascular insufficiencies are examined. The treatment of psychic disorders exhibited by quick fatigue, no patience, and insufficient performance demand special observation. According to an old tradition, the first measure taken is usually to confine patients to bed; this confinement however leads to inactivity, and should be applied only on a strictly limited basis, since otherwise the well known consequences of calcium elimination in urine and an increase in nitrogen secretion can occur. Dependency and the tendency for regression result if the action radius diminishes. It is recommended that circulation promoting drugs, physical therapy, psychopharmacy, and pharmacotherapy be employed with regard to each specific case. (Journal abstract modified)

004719 Herling, Seymore; Woods, James H. Dept. of Pharmacology, University of Michigan, Ann Arbor, MI 48109 **Mini-Symposium. IV. Discriminative stimulus effects of narcotics: evidence for multiple receptor-mediated actions.** Life Sciences. 28(14):1571-1584, 1981.

Recent studies that have utilized drug discrimination techniques to analyze the actions of narcotic analgesics and related compounds are reviewed in relation to the hypothesis that multiple receptors mediate the effects of narcotics. Studies using squirrel monkeys, rhesus monkeys, and pigeons are reviewed, and the species generality of multiple receptor models of narcotic action is evaluated. Results of studies on the discriminative stimulus effects of narcotics in rats and monkeys are consistent with the hypothesis that multiple receptors (mu, kappa, sigma) mediate the effects of these compounds. However, in the pigeon, the discriminative stimulus effects of narcotics appear to fall into only two subsets (mu and kappa agonists vs. drugs that produce phencyclidine-like discriminative effects). 70 references.

004720 Kakegawa, Norio; Sengoku, Akira; Makino, Yoshimasa; Fujiwara, Tateki; Yagi, Kazuichi. National Epilepsy Center, Shizuoka Higashi Hospital, 886, Urushiyama, Shizuoka, Japan **Polypharmacy regimen as an exacerbating risk in therapy-resistant epileptic seizures and behavioral disorders.** Japanese Journal of Child and Adolescent Psychiatry. 21(5):310-320, 1980.

Eleven children with therapy resistant epileptic seizures of various types (in spite of a polypharmacy regimen of antiepileptic drugs) were studied under inpatient care. Blood concentrations of antiepileptic drugs were monitored along with EEGs while the number and frequency of the drug doses were reduced gradually toward monopharmacy. This resulted in considerable improvement of both seizure manifestations and behavioral disorders. Some findings were: 1) in 6.1 months, as a result of decreasing the number of drugs from an averag of 6.0 to 2.9 the frequency of seizures and EEG discharges decreased; 2) behavioral disorders caused by polypharmacy disappeared with the reduction of drugs; 3) no case showed an inverse relationship between clinical seizures and behavioral disorders or forced normalization on EEGs; 4) antiepileptic drug-induced effects of the central nervous system seemed to be unspecific in nature and depend on the total amount of drugs used. 15 references. (Author abstract modified)

004721 Karczmar, Alexander G. Dept. of Pharmacology, Loyola University Medical Center, Maywood, IL 60153 **Drugs, transmitters and hormones, and mating behavior.** Modern Problems of Pharmacopsychiatry. 15:1-76, 1980.

Research on the neuropharmacology of mating behavior is reviewed, along with its immediate concomitants such as pertinent aspects of endocrinology and neuroanatomy. Emphasis is on the neuroanatomical and hormonal entities: the cortex, limbic system and the hypothalamic/hypophyseal axis on the one hand and the pituitary gland and gonads on the other. Topics include: 1) the neuroanatomical basis of mating (spinal and vascular aspects, cerebral mechanisms, effects of hypophyseal and pituitary hormones and of their interaction with neurotransmitters and drugs); 2) the general significance of hypothalamic hypophysiotropic regulatory peptides (HRPs); 3) steroidal (gonadal) hormones (feedback mechanisms, neurogenetic effects, and CNS mediated effects of the hormones on mating); 4) biorhythms and sexual activity; 5) drugs and sexual activity (including the compounds affecting monoamine activity and ovulation); and 5) aggression and sexual behavior. 356 references.

004722 Keller, William J. School of Pharmacy, Northeast Louisiana University, Monroe, LA 71209 **Catecholamine metabolism in a psychoactive cactus.** Clinical Toxicology. 16(2)233-243, 1980.

Catecholamine biosynthetic pathways in the Dona Ana cactus (Coryphantha macromeris) and its runyonii are discussed. Like peyote, Dona Ana produces and accumulates various methylated catecholamine derivatives, of which normacromerine is the most abundant. Epinephrine and norepinephrine occur naturally in the plant and serve as biosynthetic intermediates in normacromerine biosynthesis. Catecholamine precursors and derivatives have also been shown to be part of the metabolic pathway leading to the formation of normacromerine in Dona Ana. Comparison of catecholamine metabolism in humans and catecholamine metabolism leading to the formation of hallucinogenic agents in plants may suggest etiologies for certain types of mental illness. 37 references.

004723 Konig, Liesbeth; Lange, Ehrig. Medizinische Akademie Fetscherstrasse 74, DDR-8019 Dresden, German Democratic Republic /**Psychopharmacotherapy: the present state and the development of trends.**/ Psychopharmakotherapie: Stand und Entwicklungs tendenzen. Psychiatrie, Neurologie und Medizinische Psychologie. 31(10):597-605, 1979

The most common psychopharmaceuticals developed and introduced in recent years are listed, explained as to their functions, and discussed in context. The information given concentrates on the attempts to find antidepressants without cardiotoxic side-effects and psychoneuroleptics without extrapyramidal side-effects, as well as the development of long-acting or depot pharmaceuticals. The survey is restricted to psychotropics in the narrower sense, (with an antipsychotic action), and to pharmaceuticals that are produced in the German Democratic Republic or made available for clinical testing to the reporting clinic (Dresden). The report included tranquilizing substances only in special cases. (Journal abstract modified)

004724 Kristof, Miroslav. Simackova 5, 170 00 Praha 7, Czechoslovakia /**The prognosis of epilepsy and the strategy for**

terminating antiepileptic therapy./ Die Prognose der Epilepsie und die Taktik der Beendigung der antiepileptischen Therapie. Psychiatrie, Neurologie und Medizinische Psychologie. 31(8):449-457, 1979.

Basic concepts proposed by eminent epileptologists are discussed and supplemented by a specific analysis of 350 cases. On the basis of data reported in the literature and the results of personal investigations, concrete recommendations are made for the discontinuation of anticonvulsants in the treatment of epilepsy. An individual, multidimensional prognosis is considered mandatory. The pharmacotherapy of epilepsy and standards for evaluating anticonvulsant therapy are discussed. 18 references. (Journal abstract modified)

004725 Krogsgaard-Larsen, Povl. no address **Specific GABA receptor agonists and uptake inhibitors: design, development and structure-activity studies.** Chicago, Login Brothers, 1980. 195 p. $12.50.

Research on the neuropharmacology of selective GABA receptor agonists and GABA uptake inhibitors is reviewed. The role of GABA as an inhibitory transmitter and in the pathogenesis of neurological and psychiatric disorders is discussed. The use of GABA agonists, inhibitors of GABA metabolism, and GABA uptake inhibitors to increase GABA neurotransmission is reviewed. Methods used to assess GABAergic activity and selectivity are described.

004726 Leonard, B. E. Pharmacology Dept., University College, Galway, Republic of Ireland **Pharmacological properties of some generation" antidepressant drugs.** Neuropharmacology. 19(12):1175-1183, 1980.

Pharmacological properties of some second generation antidepressant drugs are described, and the clinical effects of first and second generation antidepressant drugs are compared. It is noted that the search for new antidepressant drugs has been stimulated by three main factors: 1) increasing biochemical evidence exists that some groups of depressed patients appear to show a primary abnormality in either noradrenaline (NA) or serotonin (5-HT) metabolism; 2) the discovery of drugs that show more specificity in their ability to modify either the NA or 5-HT systems; and 3) the need to produce drugs that are equally as effective as the classical tricyclic antidepressant drugs but which lack the side-effects of such drugs. It is claimed that the major clinical advantage of the second generation antidepressant drugs (nomifensine, trazadone, zimelidine, and mianserin) lies in the lack of cardiotoxicity and fewer anticholinergic side-effects rather than in improved efficacy in treating depression. 67 references.

004727 Lingjaerde, Odd. no address **Antidepressants and the serotonin uptake in platelets.** Acta Psychiatrica Scandinavica. 61(Suppl. 280):111-119, 1980.

Research concerning various aspects of the inhibitory effect of tricyclic antidepressants on serotonin uptake in platelets is reviewed. Issues discussed include: inhibitory effect on serotonin uptake in platelets vs. brain; the molecular mechanism of inhibition; inhibitory potency of different drugs; the correlation between dose and uptake inhibition; the therapeutic significance of the serotonin uptake inhibition; and serotonin uptake inhibition as a quantitative measure of antidepressant drug effect. It is concluded that the measurement of serotonin uptake inhibition in platelets has value as a research tool, while practical applicability as a guide to therapeutic is uncertain. A panel discussion of these topics is appended. 15 references.

004728 Martin, W. R. Dept. of Pharmacology, University of Kentucky, College of Medicine, Research Facility '2, MR-102, Lexington, KY 40536 **Mini-Symposium: II. Multiple opioid receptors. A little about their history and some implications related to evolution.** Life Sciences. 28(14):1547-1554, 1981.

Research studies leading to the notion of multiple opioid receptors are reviewed historically, and evolutionary implications of the notion of multiple opioid receptors and of the search for undiscovered opioid receptors are discussed. The concept that a drug could be an agonist, partial agonist, or competitive antagonist at three different receptors proved to be useful in explaining many of the differences between agonists and antagonists which had puzzled early investigators. The problems of whether there are natural agonists for all multiple opioid as well as other receptors, and whether there are potential transmitters for which there are no receptors are discussed in relation to the evolutionary potential of the human CNS. A system of receptor nomenclature is appended. 21 references.

004729 Mendelson, Wallace B.; Garnett, Debra; Gillin, J. Christian. Building 10, Room 3N224, National Institutes of Health, Bethesda, MD 20205 **Flurazepam-induced sleep apnea syndrome in a patient with insomnia and mild sleep-related respiratory changes.** Journal of Nervous and Mental Disease. 169(4):261-264, 1981.

Sleep EEG and respiratory measures were examined in a 38-year-old man with a long-standing history of insomnia and daytime sleepiness. He was found to have 7 to 18 primarily obstructive apneas per night on four baseline recordings, a finding not generally considered to be indicative of pathology. On the first two nights on which he received 30mg of the benzodiazepine hypnotic flurazepam, there were 22 and 100 apneas, and during the daytime he became extremely sleepy. Upon cessation of medication, his clinical condition improved, and the number of apneas decreased to 11 and 6 on withdrawal nights 4 and 6. Although respiratory depression is neither invariable nor unique to flurazepam, this case suggests that it may be a clinically significant problem with recommended oral doses in some individuals. 5 references. (Author abstract)

004730 Mills, Mark J. Massachusetts Dept. of Mental Health, 160 N. Washington St., Boston, MA 02114 **The rights of involuntary patients to refuse pharmacotherapy: what is reasonable?** Bulletin of the American Academy of Psychiatry and Law. 8(3):313-334, 1980.

The right of involuntary patients to refuse psychotropic medication is discussed by examining some problems raised by conflicting court decisions. It is argued that the traditional manner of treating psychiatrically ill, involuntary patients over their objections must give way to a new model in which psychiatrically determined incompetence is important. Under this model, a distinction is drawn between patients for whom the state has only a parens patriae interest and those for whom the state has some police power concern. The proposed system is designed to reallocate the present right to treatment and right to refuse treatment equities. The traditional mental commitment approach is thus altered to focus awareness onto the patient's capacity to consent. Ideally, such a system should increase psychiatric sensitivity to the perspective that what is best for the patient's illness is not necessarily best for the patient as a whole, and should reassure the mental health bar that psychiatrists are not interested in imposing treatment or acting as jailers. 92 references.

004731 Montgomery, S. A. Academic Dept. of Psychiatry, St. Mary's Hospital Medical School, St. Mary's Hospital, Harrow Road, London W9, England **Maprotiline, nomifensine, mianserin, zimelidine: a review of antidepressant efficacy in in-patients.** Neuropharmacology. 19(12):1185-1190, 1980.

Studies of the clinical efficacy of the second generation antidepressants maprotiline, nomifensine, mianserin, and zimelidine using depressed inpatients are reviewed. It is noted that the hospital inpatient trials have found maprotiline nomifensine, mianserin, and zimelidine to have the same order of antidepressant efficacy as the reference antidepressant drugs, imipramine and amitriptyline. It is noted that most of the inpatient studies are open to the criticism that they examined groups that were sometimes too small to conclude that there was no difference with the comparison drug. This methodological difficulty is exacerbated by the use of mixed, ill defined groups of depressed Ss. The advantages of the second generation antidepressants in terms of reduced side-effects and toxicity in overdose are generally well documented. 43 references.

004732 Morkovkin, V. M.; Kaplin, G. P.; Romel', T. E.; Guberman, A. S.; Mazurskiy, M. B. Moskovskaya gorodskaya klinicheskaya psikhiatricheskaya bol'nitsa No. 1 im. P. P. Kashchenko, Moskva, USSR **/The drug pathomorphosis of schizophrenia./** K voprosu o lekarstvennom patomorfoze shizofrenii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(5):745-748, 1980.

The drug pathomorphosis of schizophrenia was studied by comparing the case histories of more than 4,000 patients admitted to one psychiatric hospital in Moscow in 1951 and 1974. The clinical pictures in the preneuroleptic period and under conditions of polypharmacotherapy were compared. Results show that: the history of schizophrenia under conditions of polypharmacotherapy has changed; in polypharmacotherapy there has been an increase in attack-like forms of schizophrenia, and a decrease in continuous forms; irrespective of the character of the progress of schizophrenia there has been a significant decrease in severe catatonic conditions, delusional excitation, and pronounced stuporous states, and an increase in depressions. 22 references. (Journal abstract modified)

004733 Nestoros, J. N. Dept. of Anaesthesia Research, McGill University, 3655 Drummond St., Montreal, Quebec H3G 1Y6, Canada **Benzodiazepines in schizophrenia: a need for reassessment.** International Pharmacopsychiatry. 15(3):171-179, 1980.

Fourteen controlled clinical studies that have attempted to evaluate the usefulness of benzodiazepines in the treatment of schizophrenic patients are reviewed. Research strategies covered include: 1) comparison of benzodiazepine and placebo treatments; 2) comparison of benzodiazepine and standard neuroleptic treatments; 3) comparison of benzodiazepine, placebo, and standard neuroleptic treatments; and 4) comparison of the effect of adding a benzodiazepine to the standard neuroleptic medication to the effect of adding a placebo. It is concluded that the doses used were probably too small and inadequate to induce an ameliorating effect. However, benzodiazepines may be promising candidates for antipsychotic drugs since, by facilitating GABAergic neurotransmission, they diminish dopaminergic neurotransmission. Although higher doses will probably cause dependence, reversible addiction to benzodiazepines may be a better alternative for some subgroups of schizophrenics than the uncertain, but irreversible side-effects of traditional neuroleptics. 46 references. (Author abstract modified)

004734 Nielsen, Jorgen Achton; Biorn-Henriksen, Torben; Nielsen, Johannes. Institute of Psychiatric Demography, Psychiatric Hospital, DK-8240 Risskov, Denmark **Psychiatric illness and use of psychotropic drugs in the geographically delimited population of Samso, Denmark.** Acta Psychiatrica Scandinavica. 62(Supplementum 285):97-102, 1980.

The relationship between use of psychotropic drugs and the presence of mental illness was investigated on the island of Samso, Denmark during the 1 year period from October 1976 to September 1977. Ninteen percent of the females and 11% of the males living on the island received one or more psychotropic drugs. The amounts of psychotropic drugs prescribed averaged 18 defined daily dose (DDD) per male and 32 DDD per female. Fifty two percent of all the psychotropic drugs prescribed were given to patients with psychiatric illnesses, 18% to patients who previously had a mental illness, and 31% to people who had never been mentally ill. The amount of psychotropic drugs prescribed on Samso was one half of that prescribed in the rest of Aarhus county, due to a lower prescription rate for minor tranquillizers, hypnotics, and sedatives. 9 references. (Author abstract modified)

004735 no author. no address **Drug concentrations in neuropsychiatry.** Ciba Foundation Symposium No 74. Amsterdam, Excerpta Medica, 1980. 266 p. $45.75.

The proceedings of a symposium on plasma drug levels in psychiatry and neurology are presented. Of particular concern is the clinical value of monitoring plasma concentrations. Plasma levels are generally agreed to be important for lithium and anticonvulsants, of little value for sedative hypnotics and antipsychotic drugs, and of value in selected situations for antidepressants. The complexity and difficulties of interpretation of plasma levels in psychiatric disorders is discussed. The designated therapeutic range must be adjusted for each individual based on clinical assessment, as the therapeutic range may overlap the toxic range. The lack of quality control in some laboratories, and its consequences for the clinician are also discussed.

004736 no author. U.S. General Accounting Office, 441 G St., NW, Washington, DC 20548 **Problems remain in reviews of Medicaid-financed drug therapy in nursing homes.** Washington, GAO Report No. HRD-80-56, 1980. 87 p.

Problems facing pharmacists and registered nurses who perform monthly reviews of the drugs taken by Medicaid nursing home patients were assessed. Randomly selected nursing homes in Georgia, Iowa, Kansas, Massachusetts, Texas, and California were visited, state and federal officials were interviewed, and records and the research literature were reviewed. Based on the findings, it is suggested that medication review has not been totally effective and that pharmacists and registered nurses need ready access to a single source containing authoritative information on commonly used drugs and also a clear definition of the scope of these reviews. FDA approved drug labeling is the most widely available and widely used source of drug information; however, labeling often does not contain enough information about the proper monitoring and use of the drug. Recommendations to the Department of Health and Human Services concerning the dissemination of drug information and a medication review methodology, as well as other issues, are offered.

004737 Richelson, Elliott. Dept. of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Psychotherapeutic drugs, histamine H1 and muscarinic acetylcholine receptors.** In: Yamamura, Psychopharm. and biochem. of neurotransmitter receptors. Amsterdam, Elsevier North Holland, 1980. (p. 263-277).

The interactions of psychotherapeutic drugs with histamine-H1 and muscarinic acetylcholine receptors were studied to provide a basis for understanding some of the drugs' side-effects. Methods of assay of histamine-H1 and muscarinic acetylcholine receptors are outlined. Characteristics of histamine-H1 and muscarinic acetylcholine receptors of mouse neuroblastoma cells are described, suggesting functional and structural similarities between histamine-H1 and muscarinic acetylcholine receptors. Equilibrium dissociation constants were found for histamine-H1 and muscarinic acetylcholine receptors and a variety of psychotherapeutic drugs: antidepressants, antipsychotics, antihistaminics, and anticholinergics. One of the most interesting results is the finding of exceedingly high affinities of doxepin and amitriptyline for the histamine-H1 receptor. The results are discussed with regard to mechanism of action and side-effects of psychotherapeutic drugs. 53 references.

004738 Richens, Alan. Dept. of Clinical Pharmacology, St. Bartholomew's Hospital Medical College, London, England **Pharmacokinetics of anticonvulsant drugs.** Acta Neurologica Scandinavica. 62(Suppl. 80):40-45, 1980.

Pharmacokinetic aspects of anticonvulsant drugs which must be considered when treating epileptic patients are discussed. Specific information is presented on protein binding in anticonvulsants, protein binding interactions, and tolerance. Findings from research of folic acid treatment in epilepsy are briefly reviewed. It is concluded that an understanding of the drug handling mechanisms of the body is fundamental to a critical study the effects of drugs on the human central nervous system.

004739 Schoolar, Joseph C.; Claghorn, James L. no address **The kinetics of psychiatric drugs.** New York, Bruner/Mazel, 1979. 324 p. $19.50.

The current understanding of the usual metabolic and kinetic patterns of commonly used psychotropic drugs and their implications for treatment are examined in 16 papers presented to the 11th Annual Symposium of the Texas Research Institute of Mental Sciences, held in 1978. An overview is provided, and presentations are grouped into preclinical and clinical studies, studies with special populations (antiepileptic drugs in children, the elderly, and drug interactions). Implications for future clinical research are also examined. Focus is on biological considerations pertaining to drug action; and presentations touch on the treatment of schizophrenia, depression, manic-depressive disorder, and anxiety. Approaches to maintaining the treatment course by radioimmunoassay techniques and plasma levels are also discussed. Special considerations in the psychopharmacological management of the geriatric patient are presented.

004740 Scott, A. K.; Hawksworth, Gabrielle M. Dept. of Therapeutics and Clinical Pharmacology, University of Aberdeen, Aberdeen AB9 2ZD, Scotland **Clinical pharmacology: drug absorption.** British Medical Journal. No. 6262:462-463, 1981.

The absorption from the gastrointestinal tract of drugs used in the treatment of mental and other disorders is described, and implications for therapy are described. Absorption factors discussed include: drug formulation; gastric motility; food and fluid volume; disease; age; route of administration; and drug/drug interactions. It is concluded that many interacting factors contribute to interindividual differences in drug absorption, and that most of these affect the rate but not the extent of absorption and are important only when an immediate therapeutic effect is required. When pronounced interindividual differences in therapeutic response have been noted, these are mainly attributed to differences in metabolism or excretion, rather than absorption.

004741 Seeman, Philip. Pharmacology Dept., University of Toronto, Toronto, Canada **Brain dopamine receptors.** Pharmacological Reviews. 32(3):229-313, 1980.

The role of brain dopamine receptors as sites of neuroleptic action is reviewed. Behavioral and biochemical effects of neuroleptics are discussed in relation to the dopamine hypothesis of schizophrenia. The binding of tritiated ligands to dopamine receptors is described and differences between the D2-receptor and D1 and D3 dopaminergic sites are explained. Dopaminergic autoreceptors are discussed in relation to Parkinson's disease and the presynaptic and postsynaptic actions of apomorphine, neuroleptics, bromocriptine, and various dopamine agonists. The role of dopaminergic supersensitivity in schizophrenia, long-term neuroleptic therapy, tardive dyskinesia, and aging is considered. Directions for future research are outlined and the importance of isolating the D2-receptor is emphasized. 1278 references.

004742 Sharer, David R.; Petit, Ed. 720 Kipling '200, Lakewood, CO 80215 **Using drug holidays for chronic outpatients.** Hospital & Community Psychiatry. 32(6):420-421, 1981.

The use of a 2 day a week drug holiday from oral antipsychotic medication was evaluated in an initial sample of 27 experimental and 28 control chronically psychotic outpatients. Of the 15 patients who completed the 5 month program, 8 were in the holiday group and 7 were in the control group. For both groups, levels of self-reported and psychiatrist reported feeling and functioning were roughly the same. The holiday group's average scores increased for two of the ratings, while the control group's scores increased for all four. Despite limitations of the study, findings suggest that a 2 day a week holiday from oral antipsychotic drugs for an average period of 3.75 months did not interfere with patients' functioning. 8 references.

004743 Sholevar, G. Pirooz; Benson, Ronald M.; Blinder, Barton J. no address **Emotional disorders in children and adolescents: medical and psychological approaches to treatment.** New York, SP Medical & Scientific Books, 1980. 710 p. $60.00.

Introductory essays on disorders of children and adolescents are presented in six sections. The section on individual psychotherapy includes chapters on behavior modification and pharmacotherapy. Family therapy, group therapy, and milieu therapies are discussed in section two. A third section describes the treatment of special age groups in preschool, latency age, and adolescent categories. A fourth section on the treatment of psychosomatic disorders is followed by a fifth section on the treatment of special disorders including psychotic disorders, minimal brain dysfunction, learning disabilities, and drug abuse. A final section discusses preventative and psychotherapeutic interventions in child psychiatry.

004744 Snyder, Solomon; Goleman, Daniel; (Delorme, Marie-Raymonde, translator). Johns Hopkins University, School of Medicine, N. Wolfe St, Baltimore, MD 21205 **/The chemistry of the brain divulges its secrets./** La chimie du cerveau livre ses secrets. Psychologie. No. 130:28-34, 36, 1980.

An interview with Solomon Snyder, psychiatrist and pharmacologist well known for his work on neuromediators, is presented. Snyder's research into the brain's neuromediators has led to the possibility of developing super painkillers or memory pills. Now it is possible to determine a certain substance's receptors and to produce drugs which act on these areas alone. Although past research has been somewhat haphazard, future research can be conducted more systematically. 3 references.

004745 Strickland, Rosemary; Alston, JoAnne; Davidson, Jonathan. John Umstead Hospital, Butner, NC 27509 **The negative influence of families on compliance.** Hospital & Community Psychiatry. 32(5):349-350, 1981.

The negative influence of families on medication compliance of mental outpatients is illustrated in two case reports. Although the literature provides much evidence that family support can aid compliance, there are some indications that family members can also deter it. In the first case, a previously dependent and timid patient became more assertive at home following successful antidepressant treatment. This resulted in opposition to treatment from her husband and daughter, and the subsequent discontinuation of her medication. This was satisfactorily resolved through appropriate family counseling. In the second case, a depressed patient who become less dependent on her sister after treatment, was convinced by the sister that the medication was causing jaundice; the patient subsequently abandoned treatment and symptoms reemerged after several weeks. The family dynamics in these two cases are discussed in terms of the caretaker's perceptions of the rights and responsibilities of the sick role. 4 references.

004746 Sulser, Fridolin; Mobley, Philip L. Vanderbilt University School of Medicine, Nashville, TN 37217 **Down regulation of noradrenergic receptor function by antidepressant drugs: functional significance and distinction from antipsychotic drugs.** (Unpublished paper). Research Report, NIMH Grant 5R01-MH-29228, 1979. 8 p.

The effects of tricyclic antidepressants and of MAO inhibitors on catecholaminergic neurons in brain are reported, with emphasis on down regulation of noradrenergic receptor function by these compounds. Data are summarized which show that most, if not all, antidepressant drugs and electroconvulsive shock treatment cause a down regulation of the norepinephrine (NE) receptor coupled adenylate-cyclase system when administered chronically. This down regulation generally, but not invariably, is linked to reduction of the density of beta-adrenergic receptors. Since psychotropic drugs which can precipitate depressive illness change the sensitivity of this noradrenergic receptor system in the opposite direction, the results not only provide a further dimension of regulatory control of specific biological response, but also a scientific basis for formulation of a functional receptor pathology of affective and possibley other psychiatric disorders. 27 references. (Author abstract modified)

004747 Tennent, T. G. no address **Current trends in treatment in psychiatry.** London, Pitman Medical Publishing Company, 1980. 258 p.

The proceedings are reported for a British conference for consultant psychiatrists on current trends in treatment. Behavior therapy, neuropharmacology and psychopharmacology, medical treatment of schizophrenia, treatment of depression, sex therapy, and psychotherapy are covered. For each topic, a main comprehensive paper and two commentaries addressing the biases of the main paper are presented.

004748 Vencovsky, E.; Dobias, J. Dukelska 69, 305 99 Plzen, Czechoslovakia **/Notes on pharmacotherapy of functional psychoses./** Poznamky k farmakoterapii funkcnich psychoz. Ceskoslovenska Psychiatrie. 75(2):81-86, 1979.

The contribution of psychotherapeutic drugs to the treatment of functional psychoses is examined. It is suggested that psychopharmacotherapy has humanized psychiatric treatment, facilitated the compensation of mental disease, enabled useful contact with mental patients, and aided in their rehabilitation and resocialization. It is contended that in many instances psychopharmacotherapy restores mental patients to their former occupations and prevents the development of psychiatric invalidism. Pharmacotherapy is seen as taking its place along with two other basic approaches, psychotherapy and sociotherapy, as an integral component of treatment programs for mental patients. (Journal abstract modified)

004749 Vinar, O. K ovcinu 1519, 182 00 Praha 8-Kobylisy, Czechoslovakia **/Neuroleptics in 1979./** Neuroleptika v roce 1979. Ceskoslovenska Psychiatrie. 76(6):384-392, 1980.

Findings published in 1979 concerning the clinical use of neuroleptics are reviewed. It is concluded that there is a discrepancy between the results of controled experiments and clinical practice, and that treatment is conducted by combinations of drugs and also by insulin comas, although research has proved the superiority of monotherapy with one neuroleptic. Incisive neuroleptics for restless patients and sedative neuroleptics for apathetic patients are appropriate treatment according to some research results. The following developments are noted: haloperidol is replacing chlorpromazine as the drug of choice; the new preparations trebenzomine and clopimozid show clinical potential; dysphoria and tachycardia are predictors of adverse therapeutic effect, and dysphoria is deepened by combination with antiparkinsonian drugs; and chronic (tardive) dyskinesias are seldom persevering (irreversible). The existence of a mental syndrome due to the hypersensitivity of dopaminergic neurons in the limbic system is being considered: it is a syndrome analogous to chronic dyskinesias based on the same disorder in the striatum. Additionally, maintenance treatment currently is being studied with greater care; of decisive importance is the drug case history, appraisal of the activity of the process, and appraisal of the emotional atmosphere of the patient's family. 45 references. (Journal abstract modified)

004750 Weiss, Benjamin; Prozialeck, Walter; Cimino, Mauro. Dept. of Pharmacology, Medical College of Pennsylvania, Philadelphia, PA 19129 **Acute and chronic effects of psychoactive drugs on adrenergic receptors and calmodulin.** In: Hamet, P., Advances in cyclic nucleotide research. New York, Raven Press, 1980. v. 12. (p. 213-225).

Studies are reviewed showing that antipsychotic compounds selectively bind to calmodulin, that this binding may explain several of their biochemical actions, and that acute and chronic treatment may produce different effects. The effects that psychoactive compounds have on those biochemical mechanisms of brain influence the metabolism of cyclic nucleotides depend on whether the drugs are administered acutely or chronically. For example, antipsychotic agents acutely block the action of catecholamines on the adrenergic receptor/adenylate cyclase complex, thereby preventing the catecholamine-induced rise in cyclic AMP. But with long-term treatment, corresponding more closely to clinical use, the drugs appear to produce a compensatory increase in these catecholamine receptors. Repeated stimulation of adrenergic receptors with compounds that block the uptake of catecholamines, such as antidepressants, produces a decrease in the number of these receptors and concomitant subsensitivity to the effects of catecholamines on the formation of cyclic AMP. This is in contrast to their acute actions which result in a potentiation of the action of catecholamines. Clinically effective antipsychotic drugs also bind to an endogenous calcium dependent protein, calmodulin, found in high concentrations in the CNS. The binding can explain several of their biochemical actions and suggests that some of the pharmacological and clinical effects of these drugs may also be explained by a common mechanism. The specificity with which antipsychotic drugs bind to calmodulin suggests the possibility of searching for new and clinically more effective antipsychotic drugs based on their selective binding to calmodulin. 52 references. (Author abstract modified)

004751 Weiss, Benjamin; Wallace, Thomas L. no address **Mechanisms and pharmacological implications of altering calmodulin activity.** In: Cheung, W. Y., Calcium and cell function. New York, Academic Press, 1980. Vol. 1. (p. 329-379).

Studies are reviewed covering the distribution and biochemical actions of calmodulin, alteration of calmodulin activity by antipsychotic drugs and other substances, and calmodulin's role in the action of antipsychotic drugs. Calmodulin is an ubiquitous, calcium binding protein that regulates the activity of several calcium dependent enzymes, including specific forms of phosphodiesterase, adenylate-cyclase, and ATPase. A number of endogenous and exogenous substances have been shown to alter calmodulin's activity. The exogenous agents have in common the ability to inhibit the calmodulin-induced activation of phosphodiesterase, adenylate-cyclase, and ATPase, and many produce effects that are characteristic of antipsychotic agents. The specific mechanism by which antipsychotic drugs block the action of calmodulin apparently is by a direct, calcium dependent binding to calmodulin. This proposition is supported by the demonstration that the ability of drugs to bind calmodulin is directly related to their effectiveness in inhibiting calmodulin dependent enzymes. The binding of drugs is saturable and of high affinity and is relatively specific for agents having clinical antipsychotic activity, suggesting that calmodulin may function as an endogenous receptor for antipsychotics. A number of endogenous substances have also been found which bind to and inhibit the action of calmodulin, raising the possibility that there may be endogenous ligands in brain which function as endogenous psychotogens or endogenous antipsychotic materials. 209 references. (Author abstract modified)

004752 Wender, Paul H.; Klein, Donald F. University of Utah College of Medicine 50 North Medical Dr., Salt Lake City, Utah 84132 **The promise of biological psychiatry.** Psychology Today. 15(2):25-28, 31-34, 36, 39-41, 1981.

Advances in biological psychiatry are reviewed. While Freudian theory dominated the practice of psychiatry in the first half of the century, recent advances in research provide evidence that biological functions are central to mental illness and that much of the now entrenched psychodynamic theory is irrelevant or even misleading. Evidence for biological predisposing or etiological factors in both severe and milder forms of mental illness is cited. A review of psychopharmacological research into drug specificity is then presented; and two case studies are reported, one of panic attacks, the other of depression and low self-esteem, in which states not responsive to psychotherapy showed dramatic improvement with appropriate drug therapy. Further evidence for a biological basis for a variety of mental disorders is then examined including psychopharmacological and twin adoption studies. Also examined briefly is research into biochemical concomitants of various disorders. Major psychological sources of unhappiness are delineated; and attitudes toward biological theory and factors in public resistance to medical treatment of psychiatric disorders are discussed.

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CROSS-REFERENCE LIST

The use of a Key-Word-out-of-Context (KWOC) index, while saving time and money, poses a problem to users seeking to locate relevant references on a given topic, as all references are not found under one entry. To alleviate this problem, we have prepared the following cross-reference list.

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  - Electroconvulsive treatment
  - Electroshock
- Electroconvulsive therapy see also
  - ECT
  - Electroconvulsive shock
  - Electroconvulsive treatment
  - Electroshock
- Electroconvulsive treatment see also
  - ECT
  - Electroconvulsive shock
  - Electroconvulsive therapy
  - Electroshock
- Electroencephalography see also
  - CEEG
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  - EEG
- Electromyographic see also
  - EMG
- Elements see
  - Mineral elements
  - Names of specific elements
- Elicited see
  - Amphetamine-elicited
  - Apomorphine-elicited
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- Emergency(ies) see also
  - Medical emergencies
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- EMG see also
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- Eminence see
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- Enhanced see
  - GABA-enhanced
- Enriched see
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- Entheogenic see
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- Enuresis see also
  - Childhood enuresis
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  - Childhood epilepsy
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- Epinephrine see also
  - Adrenaline
- Episode see
  - Affective episode
  - Schizophrenic episodes
- ERG see
  - Electroretinography
- Escape see also
  - Water escape
- Estimation see
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- ET-495 see
  - Piribedil
- Ethanol see also
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- Ethyl alcohol see also
  - Alcohol
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- Euhypnos-forte see
  - Temazepam
- Evaluation see also
  - Clinical evaluation
  - Preclinical evaluation
  - Self-evaluation
- Events see
  - Behavioral events
  - Biochemical event
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  - Evidence see also
    - Behavioral evidence
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  - Evoked see also
    - Barbiturate-evoked
    - Dopamine-evoked
    - Flash-evoked
    - GABA-evoked
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    - Stimulation-evoked
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- Evoked Potential see also
  - AEP
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  - Gas exchange
- Execretion see also
  - Circadian excretion
- Experiences see also
  - Aversive experiences
  - Clinical experiences
  - Psychedelic experiences
- Exposed see also
  - Stress exposed
- Extracts see also
  - Coca extracts

F

- Facilitation see
  - Behavioral facilitation
- Factor(s) see also
  - Antihemophilic factor
  - Bass scale factors
  - Growth factor
  - Psychopharmacologic factors
  - Psychosocial factors
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  - Thyrotrophin-releasing factor
- FDA see also
  - Food and Drug Administration
- Fear see also
  - Learned fear
- Feeding see also
  - Freely feeding
- Fiber see also
  - Thin fiber
- Field see
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- Fighting see also
  - Shock-induced fighting
- Findings see
  - Preliminary findings
- Firing see also
  - Burst firing
- Fluid see also
  - Amniotic fluid
  - Crebrospinal fluid
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- Flux see also
  - Ca++-flux
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- Focus; Foci see
  - Epileptic focus (foci)
  - Epileptogenic focus
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  - FDA
- Forebrain see also
  - Anterior forebrain
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- Fragmentography see
  - Mass fragmentography
- Frequency see also
  - High frequency
- FSH see
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- Function(ing) see also
  - Affective functions
  - Autonomic functioning
  - Mixed functions
  - Sexual function(s)
  - Thyroid function

G

- GABA see also
  - Aminobutyric acid
- GAD see also
  - Glutamic acid decarboxylase
- Gain see
  - Weight gain
- Gas liquid chromatography see also
  - GLC
- GBL see
  - Butyrolactone
- GC see
  - Gas chromatography
- Generation see also
  - F1 generation
  - Second generation
- Gerbil(s) see also
  - Mongolian gerbil
- GH see also
  - Growth hormone
- Gilles de la Tourette syndrome see also
  - Tourette syndrome
- Gland see
  - Adrenal gland
  - Pineal gland
  - Pituitary glands
  - Salivary gland
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- GLC see also
  - Gas liquid chromatography
- Glutamic acid decarboxylase see also
  - GAD
- Growth Hormone see also
  - GH
- GS-385 see
  - Chloro-4-phenylsuccinimidobenzene-sulfonamide
- Guanosine triphosphate see
  - GTP
- Gum see also
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H

- H-77-77 see
  - Dimethyl-m-tyramine
- Haldol see
  - Haloperidol
- Handicapped see also
  - Intellectually handicapped
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- Headaches see also
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- Health see
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- Heart see also
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- Helplessness see
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- Hepatic see also
  - Liver
- HIAA see also
  - Hydroxyindoleacetic acid
- Histamine receptors see also
  - H1-receptors
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- Homes see
  - Nursing homes
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- Hormones see also
  - Adrenal hormones
  - Follicle-stimulating hormone
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  - Glucocortical hormones
  - Gonadotropin-releasing hormone
  - Growth hormone
  - LH
  - Luteinizing hormone
  - Melanocorticotropic hormone
  - Melanocyte-stimulating hormone
  - Names of specific hormones
  - Parathyroid hormones
  - Peptide hormones
  - Pituitary hormones
  - Sex hormone
  - Steroid hormones
  - STH
  - Thyroid hormones
  - Thyrotrophin-releasing hormone
  - TRH
  - TSH
- Hospital see also
  - Day hospital
  - General hospital
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  - Psychiatric hospital
  - State hospital
- HT see also
  - Hydroxytryptamine
  - Serotonin
- HTP see also
  - Hydroxytryptophan
- Hydergine see also
  - Dihydroxyergotoxine
- Hydrocortisone see also
  - Cortisol
- Hydroxyindoleautic acid see also
  - HIAA
- Hydroxydopamine see also
  - OHDA
- Hydroxytryptamine see also
  - HT
  - Serotonin
- Hydroxytryptaminergic see also
  - Serotonergic
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- Hydroxytryptophan see also
  - HTP
- Hydroxyvanillic acid see
  - HVA
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  - Hyperkinesis
- Hyperkinesis (ia) see also
  - Hyperactivity
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- Hypoactivity see also
  - Hypokinesia
- Hypokinesia see also
  - Hypoactivity
- Hypotensive effect see also
  - Antihypertensive effect
- H1-receptors see also
  - Histamine receptors
- H2-receptors see also
  - Histamine receptors

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- ICS see
  - Intracranial stimulation
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  - Affective illness
  - Chronically ill
  - Depressive illness
  - Lupus like illness
  - Manic-depressive illness
  - Medically ill
  - Mental illness
  - Psychosomatic illness
- IMAP see
  - Fluspirilene
- IMI see
  - Imipramine
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  - Pathophysiologic impact
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  - Clinical implications
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  - Ca++-independent
  - Na+-independent
  - Voltage independent
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  - Adrenaline-induced
  - Agonist-induced
  - Ala2-met5-enkephalinamide-induced
  - Aminophylline-induced
  - Amphetamine-induced
  - Analgesic-induced
  - Angiotensin-II-induced
  - Anticonvulsant-induced
  - Apomorphine-induced
  - Barbiturate-induced
  - Bicuculline-induced
  - Caffeine-induced
  - Cannabinoid-induced
  - Carbachol-induced
  - Carbamazepine-induced
  - Chemically-induced
  - Chloralose-induced
  - Chlorophenylalanine-induced
  - Chlorpromazine-induced
  - Chlorea-toxin-induced
  - Cimetidine-induced
  - Clonidine-induced
  - Cocaine-induced
  - Cyclophosphamide-induced
  - D-amphetamine-induced
  - Denervation-induced
  - Depolarization-induced
  - Desipramine-induced
  - Di-n-propylacetate-induced
  - Diazepam-induced
  - Dihydroxytryptamine-induced
  - Diphenylhydantoin-induced
  - Disease-induced
  - Dopamine-induced
  - Drug-induced
  - Electrically-induced
  - Electroshock-induced
  - Endogenously-induced
  - Endorphin-induced
  - Endotoxin-induced
  - Enkephalin-induced
  - Enzyme-inducing
  - Ethanol-induced
  - Exogenously-induced
  - Experimentally-induced
  - Flurazepam-induced
  - Haloperidol-induced
  - Handling-induced
  - Harmaline-induced
  - Hexobarbital-induced
  - Homocysteine-induced
  - HTP-induced
  - Hydroxytryptamine-induced
  - Insulin-induced
  - Iron-induced
  - Isolation-induced
  - Isoprenaline-induced
  - Isoproterenol-induced
  - Kainic-acid-induced
  - L-dopa-induced
  - Lesion-induced
  - Lithium-induced
  - LSD-induced
  - MAOI-induced
  - Methadone-induced
  - Methamphetamine-induced
  - Methylmercury-induced
  - Methylphenidate-induced
  - Metrazol-induced
  - Morphine-induced
  - Naloxone-induced
  - Narcotic-induced
  - Neuroleptic-induced
  - Neurotensin-induced
  - Opiate-induced
  - Organophosphate-induced
  - Pemoline-induced
  - Penicillin-induced
  - Pentobarbital-induced
  - Pentylenetetrazol-induced
  - Peripherally-induced

  - Pethidine-induced
  - Phencyclidine-induced
  - Potassium-induced
  - Psychotropic-drug-induced
  - Reflex-induced
  - Reserpine-induced
  - Schedule-induced
  - Scopolamine-induced
  - Self-induced
  - Shock-induced
  - Sound-induced
  - Stimulation-induced
  - Stimulus-induced
  - Stress-induced
  - Stretch-induced
  - Strychnine-induced
  - Sulpiride-induced
  - Tetrabenazine-induced
  - THC-induced
  - Thiazide-induced
  - Thyroid-induced
  - Tricyclic-antidepressant-induced
  - Triethyltin-induced
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  - Myocardial infarction
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  - Parasympathomimetic influence
  - Serotonergially influenced
- Infusion see also
  - Microinfusion
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  - MAOI
  - MAO inhibition(or)
  - Monoamine-oxidase inhibition(or)
- Injection see also
  - Microinjection
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- Injury see also
  - Self-injury
- Inpatient(s) see also
  - Depressed inpatients
  - Insomniac inpatients
  - Psychiatric inpatients
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- Interaction see also
  - Behavioral interactions
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  - Biological interaction
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  - Hypnotic interactions
  - Monoaminergic interaction
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  - Pharmacokinetic interaction
  - Social interaction(s)
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  - Fixed interval
- Intervention see
  - Behavioral intervention
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- Interperitoneal see also
  - IP
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  - Psychopharmacological investigation
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  - Calcium ions
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- Ionization see also
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- Iontophoresis see also
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- IP see also
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- Isolation see also
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- Isomers see also
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K

- K see also
  - Potassium
- Kidney see also
  - Renal
- Killing see
  - Mouse-killing
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L

- L-Amphetamine see also
  - Amphetamine
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  - Methamphetamine
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- L-DOPA see also
  - Dihydroxyphenylalanine
  - DOPA
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- LAAM see
  - Acetylmethadol
- Labeled see also
  - Isotope labeled
  - Spiroperidol labeled
- Lasting see
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- Learning see also
  - Maze learning
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- Level(s) see
  - High levels
- Levodopa see also
  - Dihydroxyphenylalanine
  - DOPA
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- LH see also
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- LHM see
  - Lisuride hydrogen maleate
- Li see also
  - Lithium
- LiCl see also
  - Lithium chloride
- Life see also
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- Lilly-110140 see
  - Fluoxetine
- Lithium see also
  - Li
- Lithium carbonate see also
  - Li_2CO_3
- Lithium chloride see also
  - LiCl
- Liver see also
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- Li_2CO_3 see also
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  - Biochemical localization
- Loss see also
  - Hair loss
- LSD see also
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- LU-10-171 see
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  - LH
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M

- Maladjustments see
  - Social maladjustments
- Manic-depressive see also
  - Affective-disorders
  - Bipolar
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- MBD see
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  - Biochemical measurements
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  - Autonomic mechanisms
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  - Dual mechanism
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  - Adrenoceptor-mediated
  - Agonist-mediated
  - Alpha-adrenoceptor-mediated
  - Aminobutyric-acid-mediated
  - Dopamine-mediated
  - GABA-mediated
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  - Receptor-mediated
- Medication; Medicine see also
  - Antipsychotic medications
  - Neuroleptic medication; medicine
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  - Psychosomatic medicine
  - Psychotropic medication
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- Medulla see
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  - Methoxydiisopropyltryptamine
- Merital see
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- Methamphetamine see also
  - Amphetamine
  - D-Amphetamine
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  - Methylamphetamine
- Methionine enkephalin see also
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- Method(s) see also
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- Methoxy-4-hydroxyphenylglycol see also
  - MHPG
- Methylamphetamine see also
  - Amphetamine
  - D-Amphetamine
  - Dextroamphetamine
  - L-Amphetamine
  - Methamphetamine
- Methylphenidate see also
  - Ritalin
- MHPG see also
  - Methoxy-4-hydroxyphenylglycol
- Mianserin see also
  - ORG-GB-94
- MIF see also
  - Pro-leu-gly-NH_2
- MIlk see also
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- Minnesota Multiphasic Inventory see
  - MMPI
- MK-647 see
  - Difluorophenylsalicylic acid
- MMH see
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- Model see also
  - Animal model(s)
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- Modification; Modifying; Modified see also
  - Behavior modification
  - Behaviour modifying
  - Synthetically modified
- Modulated see
  - Stress modulated
- Monitored (ing) see also
  - Holtor monitored
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- Monkey(s) see also
  - Macaca mulatta
  - Pigtail macaque
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- Monoamine oxidase see also
  - MAO
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  - MAO inhibitor
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- MT see
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- Muscle see also
  - Anococcygeus muscle
  - Cardiac muscle
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- Mutilation see
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N

- Na see also
  - Sodium
- NaCl see also
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- Nerve see also
  - Hepatic nerve
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- Neuralgia see
  - Trigeminal neuralgia

- Neurochemistry see also
  - Behavioral neurochemistry
- Neurones see also
  - Rat cortical neurones
- Neurosis see also
  - Depressive neurosis
  - Obsessive-compulsive neurosis
  - War neurosis
- Neurotransmission see also
  - Transmission
- Neurotransmitter see also
  - Transmitter
- NH_4-tyr-pro-phe-pro-$CONH_2$ see
  - Morphiceptin
- Nigrostriatal see also
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- Node see
  - Lymph node
- Noradrenaline see also
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- Norepinephrine see also
  - Noradrenaline
- Noveril; Noveril-240 see
  - Dibenzepine
- Nuclear magnetic resonance see
  - NMR
- Nucleotide(s) see also
  - Cyclic nucleotides
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- Nucleus (Nuclei) see also
  - Caudate nucleus
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O

- Observations see also
  - Biochemical observations
- Ocytocin see also
  - Oxytocin
- Offenders see also
  - Criminally insane offenders
  - Sex offenders
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- OHDA see also
  - Hydroxydopamine
- Opening see
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- ORAP see
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- Order see
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- ORG-GB-94 see also
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- Oxidase(s) see also
  - Amine oxidase
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- Papers see
  - Clinical papers
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  - Biochemical parameters
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- Parnate see
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  - Aggressive patients
  - Alcoholic patients
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  - Bipolar patients
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  - Depressive patients
  - Dysthymic patients
  - Elderly patients
  - Epileptic patients
  - Fibrositis patients
  - Geriatric patients
  - Gerontopsychiatric patient(s)
  - Hospitalized patients
  - Hyperprolactinaemic patients
  - Hypertensive patients
  - Hypothyroid patients
  - Involuntary patients
  - Manic patients
  - Manic-depressive patient(s)
  - Melancholic depressed patients
  - Mental patients
  - Mentally handicapped patients
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  - Neurotic patients
  - Parkinson patients
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  - Psychiatric patients
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  - Schizoaffective patients
  - Schizophrenic patients
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- Patterns see also
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- PCP see also
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- PCPA see
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- Pemoline see also
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  - Neuroleptic peptides
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- Performance(s) see also
  - High performance
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  - Behavioral pharmacology
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  - Behavioral pharmacotherapy
- Phencyclidine see also
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- Phenethylamine see also
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- Phenylethylamine see also
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- Picture see
  - Clinical picture
- Pills see also
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- Placebo see also
  - Double placebo
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  - Evoked potential(s)
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- Practitioner(s) see
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  - Behavioral predictors
- Preparations see
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- Pressure see also
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- Primed see
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- Probe(s) see also
  - Pharmacologic probes
  - Pharmacological probes
- Problem(s) see
  - Methodological problem
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- Procedures see also
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- Process see
  - Creative process
- Processing see also
  - Information processing
- Prone see
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  Manic-depressive psychosis
  Manic psychosis
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Pump see
  Lithium-pump
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Q

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  Leeds-Sleep-Evaluation-Questionnaire

R

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  Domperidone
Radiation; Ray see
  Gamma radiation (ray)
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  Dopamine radioreceptor
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  Aminobutyric acid receptor(s)
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  Beta-adrenergic receptor(s)
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  Cholinergic receptor(s)
  Delta-receptor(s)
  Diazepam receptor
  Dopamine receptor(s)
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  Drug receptors
  Enkepalin receptors
  GABA receptor(s)
  Glucocorticord receptor
  Glutamate receptors
  Histamine receptors
  HT receptor
  HTP receptors
  Hydroxytryptamine receptors
  H1-receptor(s)
  H2-receptor(s)
  Ionophore receptor
  Kappa-receptor(s)
  Monamine receptor(s)
  Monoaminergic receptor
  Mu-receptors
  Muscarinic receptor(s)
  Neuroleptic receptor(s)
  Neuropeptide receptor
  Neurotensin receptor
  Neurotransmitter receptor(s)
  Nicotine receptors
  Noradrenaline receptors
  Noradrenergic-alpha2 receptors
  Norepinephrine receptor
  Opiate receptor(s)
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  - Postsynaptic receptors
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  - Progestin receptors
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  - Serotonergic receptors
  - Serotonin receptor(s)
- Recorded see
  - EMG recorded
- Redergine see
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